

**UTILITY OF CHEMOPORT IN PAEDIATRIC
ONCOLOGICAL PATIENTS, A SURGICAL PERSPECTIVE**

**A DISSERTATION SUBMITTED TO THE TAMILNADU DR.
M.G.R. MEDICAL UNIVERSITY, CHENNAI, IN PARTIAL
FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF
M.Ch PAEDIATRIC SURGERY**

August 2014

CERTIFICATE

This is to certify that the dissertation entitled “Utility of Chemoport in Paediatric
Oncological patients, a surgical perspective” is the bonafide work of

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*UTILITY OF CHEMOPORT IN PAEDIATRIC ONCOLOGICAL
PATIENTS, A SURGICAL PROSPECTIVE*

INTRODUCTION

A totally implantable access device or 'chemoport' is a small medical appliance that is installed beneath the skin. A catheter connects the port to a central vein with a large inflow of blood. Under the skin, the port has a septum through which drugs can be injected and blood samples can be drawn repeatedly, usually with far less discomfort for the patient than a more typical "needle stick".

Ports are used mostly to treat oncology and hematology patients, but recently ports have been adapted also for hemodialysis patients. But, in our institute we use it for various paediatric oncological diseases.

In this retrospective study, we try to study the number of patients who underwent chemoport insertions, the duration for which the chemoport was in situ and the number of patients who successfully completed chemotherapy. We have tried to study the chemoport related

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Utility of Chemoport in Paediatric oncological patients, a surgical perspective.

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We approve the project to be conducted as presented.

Yours sincerely

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ABSTRACT

Title: Utility of Chemoport in Paediatric Oncological patients, a surgical perspective.

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Degree and Subject: M.Ch. Paediatric Surgery

Name of the Guide: Dr John Mathai.

Aim/Objectives:

To assess the utilization, indications for insertion, removal and risk factors responsible for the premature removal of the chemoports.

Materials and Methods:

All children who underwent chemoport insertion between January 2007 and December 2013 were included in this study. This was a retrospective study. The details of eligible patient were obtained from the clinical work station and centenary block operation register. Data were analysed using 2*2 tables for odd's ratio and chi square test was employed to know the significance of the risk factors with the use of SPSS software version 1.6.

Results:

239 children were studied for the period between January 2007- December 2013. 69 of the children had completed treatment, 97 were still undergoing chemotherapy, 32 had complications like infection, thrombosis, extravasation, broken catheter and hematoma, deaths were seen in 17 children with chemoport in situ and 24 were lost to follow up. The median duration for which chemoport remained in situ including those

with complications was 273 days. Amongst the risk factors leading to premature removal of the chemoport studied namely; pre insertion chemotherapy, duration of surgery, seniority of the surgeon, serum albumin, prothrombin time, INR, Platelet count, total count and absolute neutrophil count at insertion. Absolute neutrophil count was the sole factor that reached statistical significance with a P value of 0.03.

Conclusion:

Chemoport is a good tool for vascular access in paediatric cancer patients requiring long term chemotherapy. Chemoports are not without complications. The most common complications are infectious complications amounting to 10.87% of our study population. Absolute neutrophil count <500 cells/microlitre is a strong predictor of complications with chemoport at any stage of chemotherapy.

Key words: Chemoport, thrombosis, infection, absolute neutrophil count.

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INTRODUCTION

A totally implantable access device or 'chemoport' is a small medical appliance that is installed beneath the skin. A catheter connects the port to a central vein with a large inflow of blood. Under the skin, the port has a septum through which drugs can be injected and blood samples can be drawn repeatedly, usually with far less discomfort for the patient than a more typical "needle stick".

Ports are used mostly to treat oncology and hematology patients, but recently ports have been adapted also for hemodialysis patients. But, in our institute we use it for various paediatric oncological diseases.

In this retrospective study, we try to study the number of patients who underwent chemoport insertions, the duration for which the chemoport was in situ and the number of patients who successfully completed chemotherapy. We have also tried to study the chemoport related complications and reasons for removal of the chemoport.

AIMS AND OBJECTIVES

To study the utilisation of totally implanted devices or chemoporters in paediatric oncology patients.

The outcomes being studied were:

A. Utilisation of totally implanted devices or chemoporters in this services

1. Number of ports inserted annually.
2. Break down for insertion by oncological diagnosis.

B. The Life span of the ports:

1. Duration for which port remains implanted.
2. Number of successful completion of chemotherapy with ports.
 - Break down as per diagnosis.
 - Number still undergoing chemotherapy without complications.

C. Chemoport intolerance and the identification of etiological association;

1. Temporal relationship between occurrence of device intolerance and duration of chemotherapy.
 - a. Number of days since insertion of device.

2. Cause for port complications.

a. Infectious.

i. Etiological agent and sensitivity pattern of isolates.

ii. Clinical syndrome of septic complication:

Local infection: catheter tunnel/port pocket

Systemic sepsis syndromes: Bacteremia/septic shock/MODS

b. Thrombosis.

c. Port Malfunction.

Occlusion/disconnection/peripheral access failure/ extrusion/ fracture

d. Other reasons for adverse outcomes.

i. Surgical complications at insertion.

ii. Complications at removal.

3. Risk Factors for complication requiring removal.

a. Insertion occurred at diagnosis or after administration of chemotherapy through peripheral access.

b. Seniority of surgeon.

c. Surgical procedure duration.

d. White cell count/ ANC at insertion.

e. Albumin.

f. PT/ INR/ Platelets

D. Port Removal

a. Number of chemoports removed.

b. Indication for removal.

c. Time since insertion.

d. Complication of removal.

E. Framing of guidelines for best medical practice in our setup.

REVIEW OF LITERATURE

The single most frequent operation that the surgeon performs for a child with malignancy, is for vascular access, for the administration of chemotherapy (1).

Treatment of childhood malignancies has become more complex and sophisticated employing a multidisciplinary approach. It calls for repeated cycles of chemotherapy with the attendant problems of systemic toxicities, immunosuppression and thrombosis which result in difficulties with venous access. As a consequence, centrally placed, long term venous catheters have gained widespread acceptance for the administration of chemotherapy, antibiotics, total parenteral nutrition, blood products and blood sampling, without causing much pain (2).

There are two types of centrally placed long channels in use-

- 1) Tunneled external catheter.
- 2) Totally implantable access device or chemoport.

Tunnelled external catheters are easy to access, less expensive, are associated with less extravasation into subcutaneous tissue. They allow for more rapid infusion and can be removed on an out patient basis without the need for anaesthesia. Totally implantable ports are more cosmetic, less prone to infection as they lie beneath the skin. They are low on maintenance and cause less restriction to physical activity.

Even though they are generally considered safe and effective for the administration of chemotherapy, these devices are not without risks and complications. It has become the standard of care in many of the centres dealing with paediatric oncology

on a large scale. These long channels are prone to complications like dislodgement, thrombosis and infection (1, 2). However, the knowledge regarding the care and maintenance of these centrally placed lines has to be defined for each centre taking into consideration their unique situation.

External Tunneled Catheters

Historically, the first experience of the use of central venous access was by Dudrick and coworkers in 1968. A polyvinyl catheter was inserted into the external jugular vein which was then threaded into superior vena cava. But, the catheter was stiff and lead to significant thrombotic and infectious complications. The use of a more flexible silicone rubber catheter was reported by Broviac and coworkers in 1973. Silicone rubber leads to less thrombosis and is chemically inert. It was 90 cm long with a Dacron cuff which was 30 cm from the catheter hub. The catheter was tunneled subcutaneously from the site of venous access usually by a cephalic cut down onto the anterior chest wall and the cuff was placed proximal to the exit site. The vita cuff around the catheter promoted the fibrous tissue ingrowth and was believed to decrease the complications like infection and dislodgement of the catheter (2).

Hickman and colleagues modified the design of catheters for the use in children undergoing bone marrow transplantation in 1979. Hickman's catheter had a thicker wall and 0.1mm diameter more to allow for blood sampling as well as administration of chemotherapeutic agents.

The success of the external tunneled catheters is well known and they are the most common form of vascular access in children. They can be single lumen or multiple lumen

external tunneled catheters. The sizes vary from 0.27F for premature neonates to 14F for older children. Painless access is the main advantage. However, they have several disadvantages when used for prolonged periods such as; altered body image, interference with play and leisure activities like swimming. In addition, they require periodic flushing and regular dressings. They are also prone to colonization by skin organisms and hence are not recommended for chemotherapeutic schedules lasting more than one month (3).

Totally implanted Devices or chemoport

A port consists of a reservoir compartment (the portal) that has a silicone diaphragm for needle insertion (the septum), with an attached tubing (the catheter) (4). The origin of the ports dates back to the attempts at using the existing devices from other specialities to provide venous access in cancer affected children. Hydrocephalic shunt was used for parenteral nutrition in an infant for a 22 month period by Belin and coworkers. Long term intrahepatic chemotherapy for unresectable hepatic tumour was devised by Fortner and Pahnke with the use of an Ommaya reservoir (2).

The device is surgically inserted under the skin in the upper chest or in the arm and appears as a bump under the skin. It is completely internal and affords the patient considerable freedom to enjoy bath and pursue outdoor activities like swimming once the wound has healed. The catheter runs from the portal and is surgically inserted into a vein (usually the internal jugular vein in our institution). Ideally, the catheter terminates in the superior vena cava, just upstream of the right atrium. This position allows infused agents to rapidly reach all parts of the body (4).

The septum is made of a special self-sealing silicone rubber; it can be punctured hundreds of times before it weakens significantly. To administer treatment or to withdraw blood, a health professional will first locate the port and disinfect the area. Then he or she will access the port by puncturing the overlying skin with a 90° Huber point needle, although, a winged needle may also be used. (Due to its design, there is a very low infection risk, as the breach of skin integrity is never larger than the caliber of the needle. This gives it an advantage over indwelling lines such as the Hickman line). Negative pressure is created to withdraw blood into the syringe, to check for blood return and to see if the port is functioning normally. Next, the port will be flushed with a saline solution.

Then, the treatment will begin. After each use, a heparin lock is made by injecting a small amount of heparinized saline into the device. This prevents development of clots within the port or catheter. In some catheter designs where there is a self-sealing valve at the far end, the system is locked with just saline. The port can be left unaccessed for as long as required. The port is covered in a dressing while in use to protect the site from infection and to secure the needle in position (4).

Ports have many uses in cancer patients:

- To deliver veno-irritant chemotherapy to cancer patients who must undergo treatment frequently. Chemotherapy is often toxic, and can damage skin and muscle tissue, and therefore should not be allowed to extravasate into these tissues. Chemoports provide a solution for delivering drugs quickly and efficiently through the entire body via the circulatory system.

- To deliver total parenteral nutrition in those unable to take (adequate) food orally for a long period of time.
- To deliver coagulation factors in patients with severe coagulopathy.
- To withdraw (and/or return) blood in patients who require frequent blood tests.
- To deliver antibiotics to patients requiring them for a long time or frequently.
- For delivering radiopaque contrast agents, which enhance contrast in CT imaging (4).

Insertion techniques

Selection of the vein for central venous access is dependent on the individual surgeon's preferences. Most common veins used for vascular access are subclavian, external jugular and internal jugular vein. Alternative veins include the common femoral, the great saphenous vein, inferior epigastric vein and the inferior vena cava through the trans lumbar and trans hepatic routes, the intercostal veins and the azygous vein (5-11).

However, the requirement for a firm bony surface to place the reservoir precludes most of these options except for the large veins of the neck.

Insertion in internal/external jugular vein

Internal jugular vein lies on the lateral side of the triangle formed by the heads of the sternocleidomastoid muscle, just beneath the sternocleidomastoid muscle. The right internal jugular vein follows a straight path before entering the right atrium, while the left

enters the junction of the confluence of the subclavian and innominate veins at right angle. The external jugular vein makes an entry into the subclavian vein at a right angle which means the catheter must make an angle to enter the subclavian vein (2).

Procedure is normally done in the operating room with general endotracheal anaesthesia. Fluoroscopy at the time of insertion is useful to confirm the position of the catheter. A roll is placed under the child's shoulder and neck extended and turned towards the opposite side for adequate access to internal jugular vein/external jugular vein (IJV/EJV). The insertion can be done through percutaneous technique (Seldinger) as well as through a cut down technique for assessing IJV/EJV (2). An incision, midway between the clavicle and the ramus of the mandible is made and the vein is identified. A transverse incision is made in the chest away from the nipples and the port placed in the plane between the fascia and the muscles. It is fixed using non absorbable sutures. The catheter is tunneled subcutaneously into the neck on the lateral part of the incision made in the neck. In the case of EJV, proximal end can be ligated and the vein is assessed. If IJV is planned a venotomy is done and the catheter is introduced without the ligation of the proximal limb. The position of the catheter is confirmed using fluoroscopy. Skin incisions are closed using absorbable sutures.



Figure 1 Position of the child for chemoport insertion



Figure 2 Isolation of Internal jugular vein

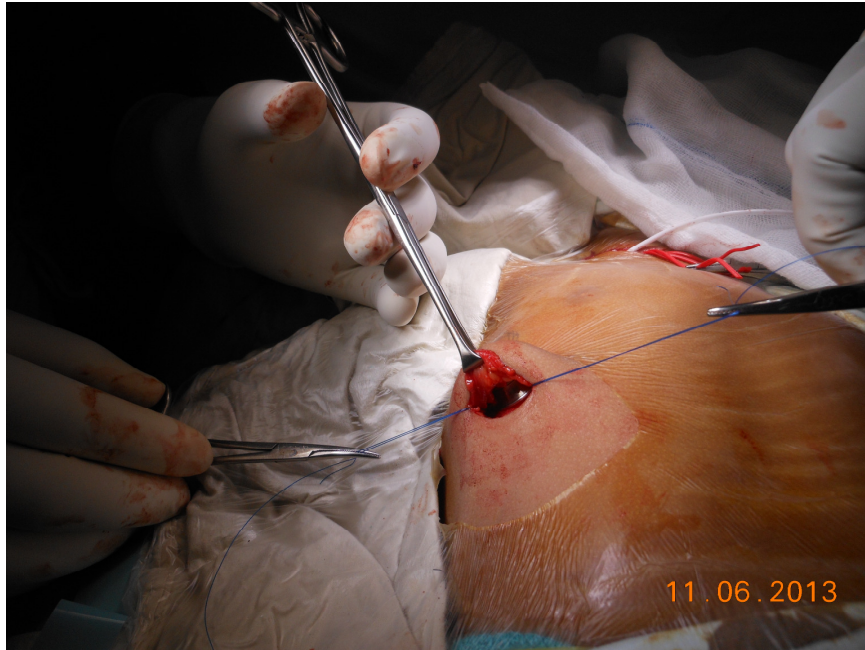


Figure 3 Placement and fixation of the port in the chest



Figure 4 Catheter introduction into the internal jugular vein

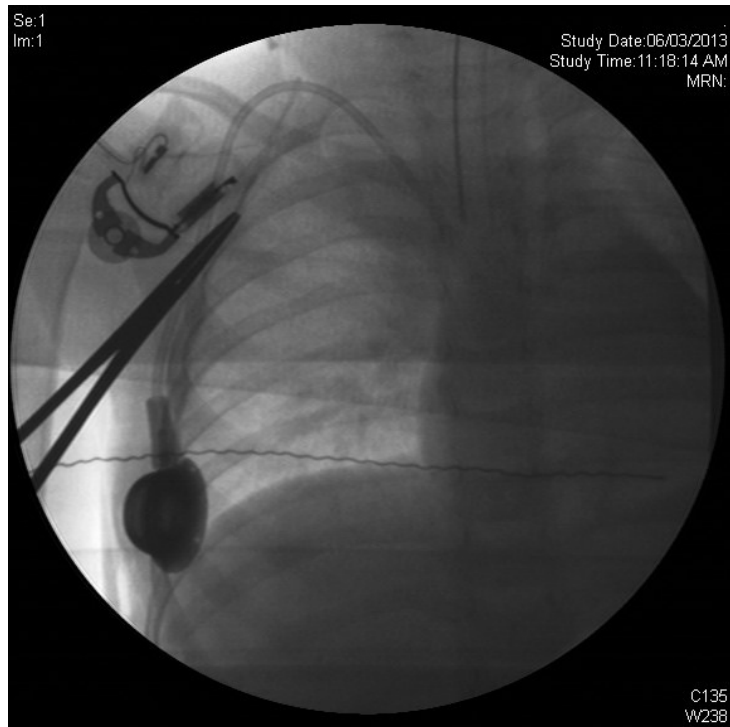


Figure 5 Confirmation of the position by fluoroscopy



Figure 6 Post operative picture showing the port as a BUMP under the skin

Insertion in subclavian vein

The position of the patient and the anaesthesia techniques remains the same as for IJV/EJV insertions. The subclavian vein is accessed via infraclavicular approach with an 18G needle. Skin incision is made in the chest wall anteriorly and the catheter is tunneled subcutaneously into the exit of the guide wire which passes over the 18G needle and left in situ. The port is fixed through the lower incision and the catheter is trimmed to appropriate length and the position confirmed by fluoroscopy (12).

Complications

Complications with the chemoport can be classified into

- intraoperative
- post operative complications.

Infection and occlusion are the most frequent complications associated with vascular access devices (VAD) (13). Extravasation, hydrothorax and cardiac perforation are less common complications but they are as serious as infections that lead to removal of the devices (14, 15, 16).

Complications of the chemoport insertion can be varied from local infection to SIRS (requires its surgical removal) to a malposition when intraoperative imaging is not used. Other complications which can arise are; infection, thrombosis of the port, mechanical failure in which the system may break, pneumothorax and arterial injury which almost always compel its removal (1). Preset criteria for the diagnosis of device

related infections morbidity were defined using the following criteria: 1) a 10-fold or greater increase in colony forming units of organism per millimeter of blood obtained through the device, compared with simultaneous peripheral blood cultures 2) in the absence of peripheral blood cultures, more than 100 colony forming units of organism obtained through the device and 3) a positive result of catheter tip culture when the device was removed specifically for suspected device related infection, in the absence of cultures as stated above. Device related bactremia or fungemia was considered cured when culture results were negative at the termination of antibiotic therapy and no evidence of clinical infection occurred atleast 2 weeks later. Cutaneous site infection was defined as erythema, induration or tenderness and exudates at the catheter cutaneous port surface needle access site (17).

Infection rates and definitions of catheter related infections are defined in different ways in different institutions. A study of 1100 central devices by Children Cancer Study Group noted 8.5%- 31% patients required removal because of infection (18). When the isolation of bacteria from two different sites as well as from the tip is same then it is defined as catheter related bacteremia (3, 19)

The most common organism isolated from the catheter related infection is the coagulase negative staphylococci (CONS) (18). Other organisms which lead to catheter related infection are klebsiella pneumoniae, streptococcus viridans, group D Enterococcus, Staphylococcus aureus and Escherichia coli (20, 21). One of the ways to inhibit the bacterial colonization in the catheter is by modifications in the construction. Antibiotic bonding to the catheters have been shown to decrease the amount of

colonization (22). Skin entrance site of the catheter is believed to be the site of origin of catheter related infections. Bacteria multiply, advance along the catheter and finally gain access to the blood stream (23).

Whenever there is a diagnosis of catheter related infection, controversy regarding keeping the catheter in situ or removal arise. Current recommendations include leaving the catheter in situ, antibiotic administration through the port and a repeat blood culture in 24-48 hours. Those who respond to this will be given therapy for 14-21 days. Those who do not respond require the removal of the catheter (3).

Catheter related infections may not respond to antibiotic therapy because of the thrombus at the tip of the catheter where the bacteria or fungus colonize. If a thrombus is identified or suspected, a bolus of urokinase in normal saline should be infused through the catheter and repeated 24 hours later. Patients who fail to this therapy warrants removal of the catheter (24).

The incidence of catheter related fungal infections was 2.7% from 43 cases studied in 11 various series. *Candida tropicalis* and *albicans* attach more extensively to polyvinyl chloride (PVC) in central catheters than to the peripheral lines which have Teflon. Treatment is amphotericin B and removal of the catheter (25, 26)

Occlusion

The common mechanical problem that occurs as a result of thrombus around the tip of the catheter, is the occlusion of the catheters. Others are, precipitation of poorly soluble fluid components (27) or an obstruction seen in the subclavian catheters near the level of the first rib. The placement of the thrombus at the right atrium not only affects

the catheter function but also attributes to complications such as clot dislodgement, pulmonary embolism and vessel thrombosis. Urokinase has been used to treat occlusion caused by thrombus in a variety of dosing regimens (28, 29, 30).

A study on study of “Feasibility and Acceptability of Subcutaneous Implantable Ports in Cancer Patients” by Mittal L, Kalra M and Mahajan A in New Delhi observed complications like infection (4%), port fracture (4%), Thrombosis of the catheter (1%) and blockage in 1% of patients (31).

There are various methods of maintenance of ports and tunneled catheters and have been individualized for each hospital. Care of the chemoport at home includes simple steps- Keep the site covered clamped and clean, changing the dressing every 7 days.

While accessing the port, simple steps should be followed like washing the hands with a sanitizer before accessing the port, cleaning the area of the port with an antiseptic solution, flushing before and after administration of the chemotherapy and putting a sterile dressing after the administration of the chemotherapy (3, 32). Reservoir accessed through the skin which can be painful and removal of the port requires an operative procedure which will subject the child to anaesthesia which are the main disadvantages.

Low profile P.A.S port is an addition to the port which is placed in the forearm through basilic vein or cephalic vein. But, it has the disadvantage of being a very small port; it will be difficult to access in children with a lot of overlying soft tissue (2, 33).

Comparison of External tunneled catheters (EC) and chemoport (TID)

Chemoports require less frequent cleaning, flushing and are subcutaneous and thus expect to be lower risk of complications when compared with ECs. Several studies have shown a significant lower infection rates with chemoports than ECs (34, 35).

The Children Cancer Study Group review found that ECs were removed more frequently than chemoports for infection, but no data comparing the number of complications per catheter day of use were given (19). Comparison between EC and chemoports is difficult. Majority of the data implies that chemoport associated with less infection. But, ECs are inserted more frequently, which attribute to the higher rate of infection.

Table 1 Advantages of EC versus chemoports (TIDs) (2)

External tunnelled catheter	Chemoports
Easier to access	Improved cosmetic result
Less expensive than ports	Less restriction to normal activities
Pose less risk for extravasation into subcutaneous tissue	Less maintainence care
Allow more rapid infusion	Well protected
Can be removed at bedside	Lower risk of infection

Patient and Family acceptance

Acceptance of the family and the patient is an important aspect in deciding which vascular access device (VAD) to use. Questionnaires were obtained at 3 and 12 months post insertion by Poole and coworkers following insertion of external catheters (EC) and totally implanted devices (TID) or chemoports. There was a positive response to both EC and chemoport insertions. The only negative answers were regarding the daily change of dressing in the case of EC's and the pain associated while accessing the chemoports. Even though patients experienced pain with chemoports, they strongly recommended chemoports as a vascular access for the administration of chemotherapy (2).

MATERIALS AND METHODS

a. Inclusion criteria

All the children who underwent chemoport insertion between January 2007-December 2013 in the Department of Paediatric Oncology will be included in the analysis.

b. Exclusion criteria

Children who underwent chemoport insertion elsewhere but taking chemotherapy in CMC hospital will be excluded.

Historical:

Details regarding age, gender, diagnosis , date of insertion, duration of the chemoport in situ, date of removal, reasons of removals, seniority of the surgeon, duration of surgery and complications of the chemoport will be obtained from the Centenary Block Operating Room register, clinical work station and IP charts.

Laboratory:

Total counts, Absolute neutrophil count, blood culture, catheter tip/pus culture, Prothrombin time, INR, serum albumin and platelet count reports will be obtained from the clinical work station.

Outcomes measured:

Duration of the chemoport, the number of patients who successfully completed chemotherapy, complications of chemoport insertions, risk factors for chemoport related adverse events.

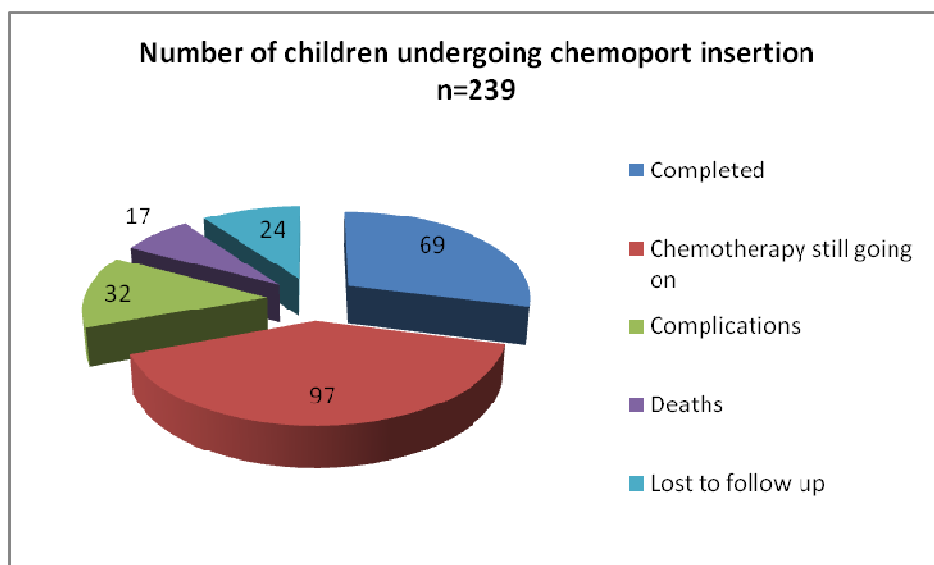
Demographic details, oncological diagnosis, date of insertion and removal of chemoport will be obtained from the operation register maintained in the Centenary Block operating room in CMC Hospital, Vellore. All the details of chemotherapy completion, surgery details and the investigations will be obtained from the clinical work station. Adverse events will be obtained from the surgical and consultation records in clinical work station and IP records.

Odd's ratio will be calculated in 2*2 tables. P value will be calculated using the chi square test to know the significance of the risk factors with the use of SPSS software version 1.6.

RESULTS AND ANALYSIS

Figure 7

Distribution of chemoport in our cohort

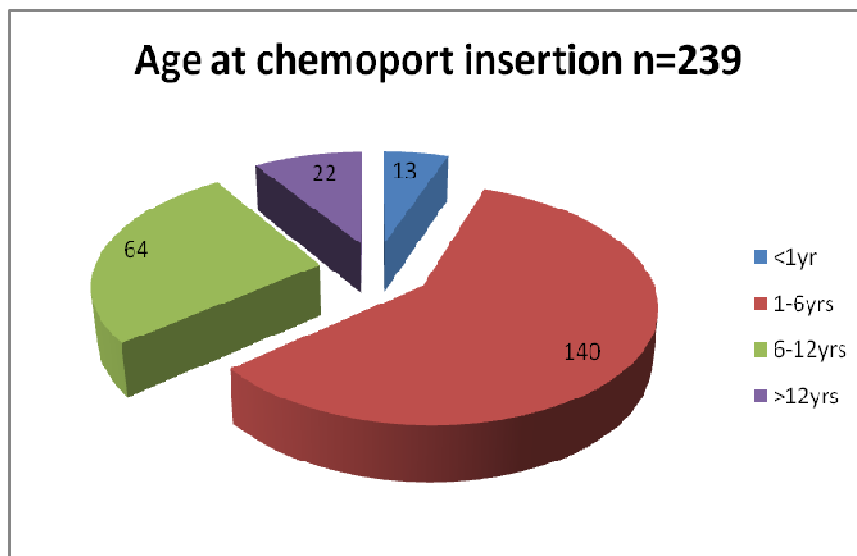


In our cohort of 239 children, 101 had to be removed. Of these, there were a total of 69 who completed chemotherapy successfully with the chemoport in situ, 32 had complications with the chemoport in situ. 97 are undergoing chemotherapy, 17 deaths with chemoport in situ and 24 were lost to follow up after insertion of chemoport, at the end of the study as on 31/12/2013.

Table 2

Age at Chemoport insertion

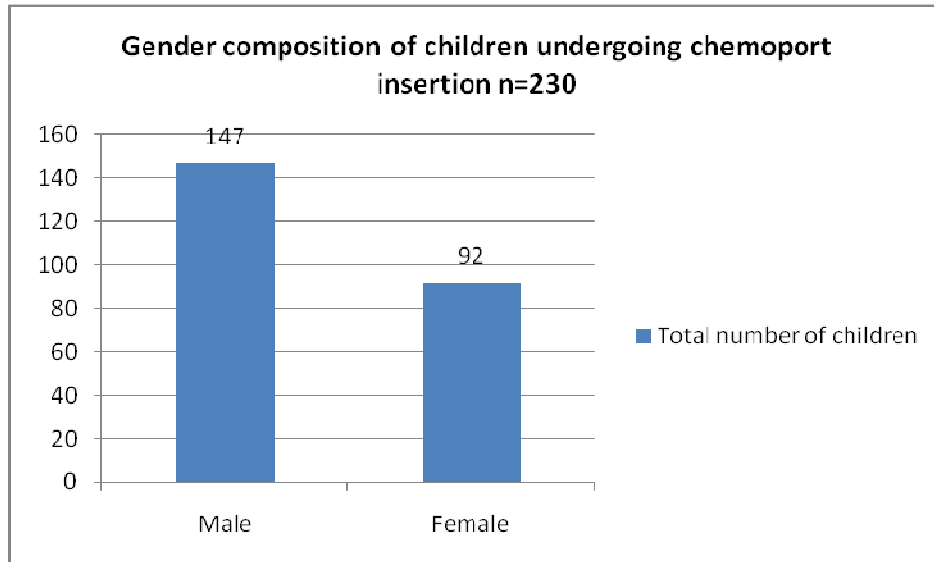
Age	Number of children
<1yr	13
1-6yrs	140
6-12yrs	64
>12yrs	22
Total	239



Youngest child in which chemoport was inserted was 21 days. Oldest child was 17 years. 59% of the children were in the age group of 1-6 years and 5% of the children were less than 1 year.

Figure 8

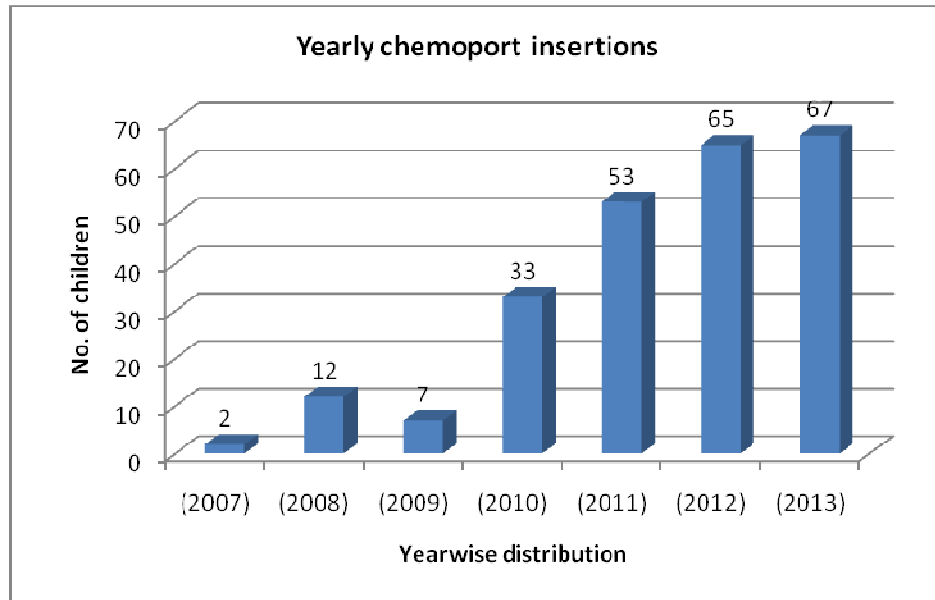
Gender composition of children undergoing chemoport insertion



Total number of males were 148(62%) children and 91(38%) were females out of 239 chemoport insertions.

Figure 9

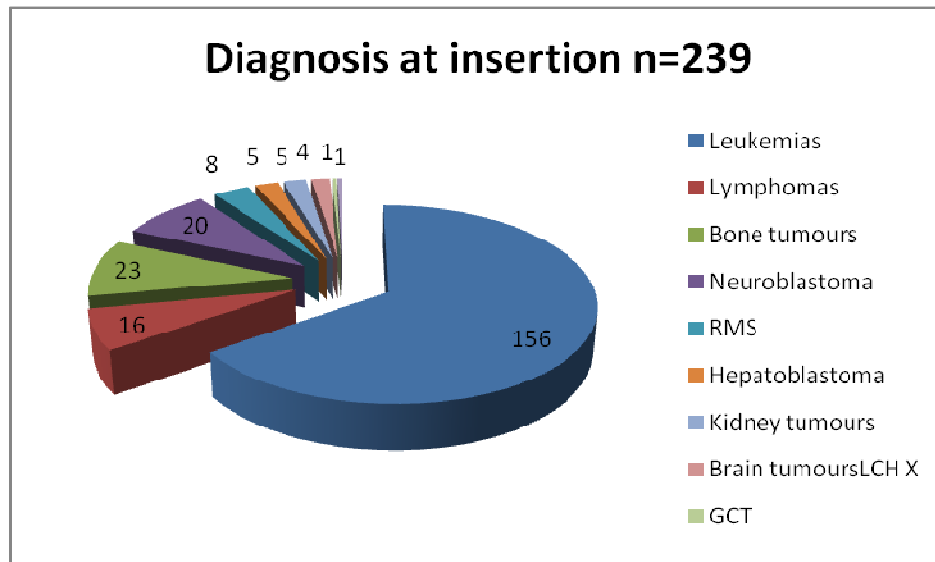
Yearly chemoport insertions



There was a steady increase in the number of chemoport insertions from 2007-2008 with 67 of the chemoports out of 239 were inserted in the year 2013.

Figure 10

Oncological diagnosis at insertion



Majority of the chemoport insertions were done for lymphoproliferative disorders mainly leukemias amounting to 172 out of 239 children constituting 72%. Most common solid tumours for which chemoport was inserted were bone tumours and neuroblastoma. Solid tumours accounted for 66 out of 239 children who underwent chemoport insertions.

Table 3

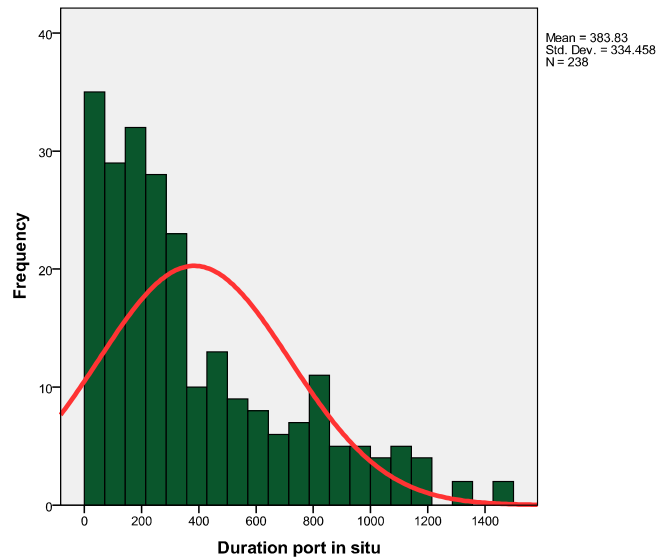
Duration of chemoport

Duration (days)	Successful performance of chemoport	Complicated inclusive of death with chemoport in situ	Total
<500	106*	32 (16)	154
500-1000	41	2** (1)	43
1000-1500	18	-	18
Total	165	50 (17)	215

Note: Bold figure within brackets under the heading complications denote death

* 1 child developed sepsis after the completion of chemotherapy.

** Neck broken during the chemoport removal on table.



154, 43, and 18 children were in <500, 500-1000 and 1000-1500 days respectively with the port in situ. The recorded number of days for which the chemoport was in situ ranged from 2 to 1461 days (mean 383.8 days). The shortest duration was 2 days (this patient was lost to follow up). Among those who successfully completed chemotherapy, the port was in situ between 77-1432 days (median 411.5 days). **The median number of days for which the chemoport remained in situ including those who had complications was 273 days.**

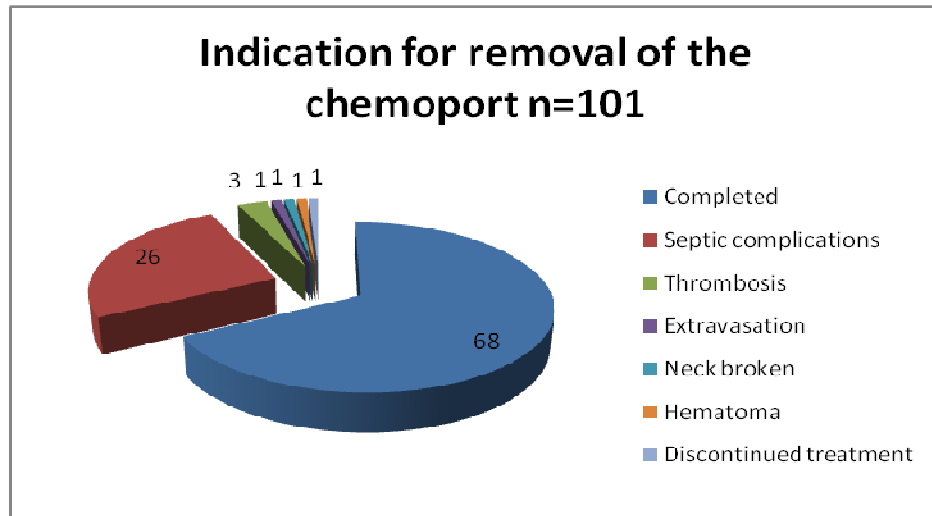
Table 4

Indications for removal of chemoport

Indication	Number
Completed	68 *
Septic complications	26
Thrombosis	3
Extravasation	1
Neck broken	1 **
Hematoma	1
Discontinued treatment	1
Total	101

* 1 child had sepsis after 6 days the completion of chemotherapy.

** The neck broke at removal of chemoport after completion of chemotherapy.



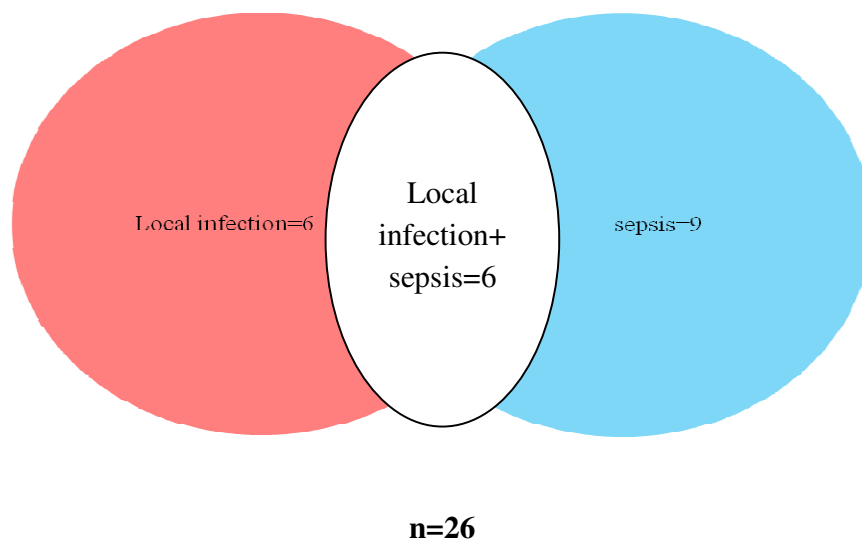
Most common indication for the removal of the chemoport was completion of chemotherapy accounting to about 67%. The most frequent complication occurred was the infection in the form of local infection/ sepsis which occurred in 26% of patients that resulted in premature removal of the chemoport.

Table 5

Infection leading to removal

Type of infection	Total number of children
Local infection	11
Sepsis	9(1-completed+sepsis)
Local infection+sepsis	6
Total	26

Figure 11 Infection leading to removal



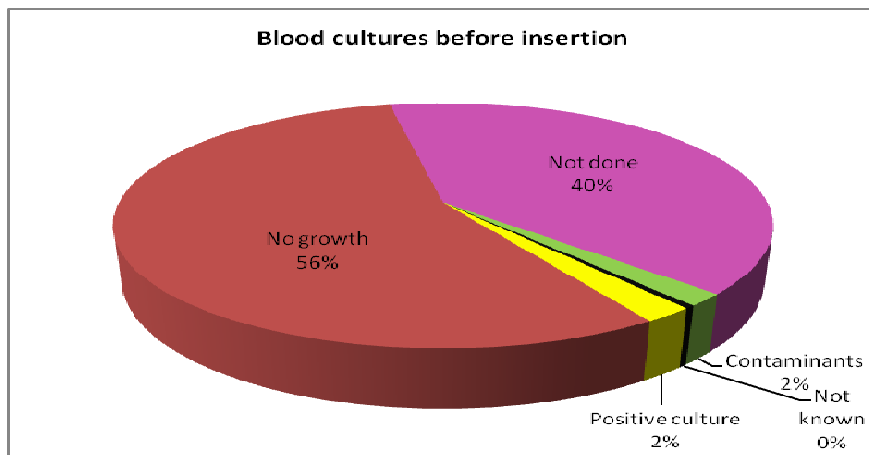
Local infection was seen in 11 out of 26 (42.4%) children and sepsis was seen in 9 out of 26 (34.6%) children who had infection as an indication for removal. 6 out of 26 (23%) children had local infection with sepsis which required chemoport removal.

- Local infection was considered when there was erythema, induration, tenderness or discharge from the port insertion site.

Table 6

Blood cultures before insertion

Culture	Total number of children
Positive culture	5
No growth	133
Not done	95
Contaminants	4
Not known	1
Total	239



Positive cultures before insertion was seen in 2% of the children and 56% of the children had no growth on blood culture before the insertion of the chemoport.

Table 6(a)

Blood culture	Successful utilization of	Complicated inclusive of death	Total
Culture positive	3	2	5
Culture negative	71*	18	89
Total	74	20	94

* Included neck broken and 1 sepsis.

On analyzing blood cultures before insertion, 5 were culture positive and 89 were culture negative among the total of 94 children. 3 were in the successful utilization of chemoport group and 2 were in the group of complications out of 5 children who had culture positive before insertion.

71 (79.77%) were in the successful utilisation of chemoport group and 18 (20.22%) were in the group with complications out of the 89 children who had culture negative before insertion. Odd's ratio of 0.75 with a confidence interval between 0.36-1.55 and P value was 0.29.

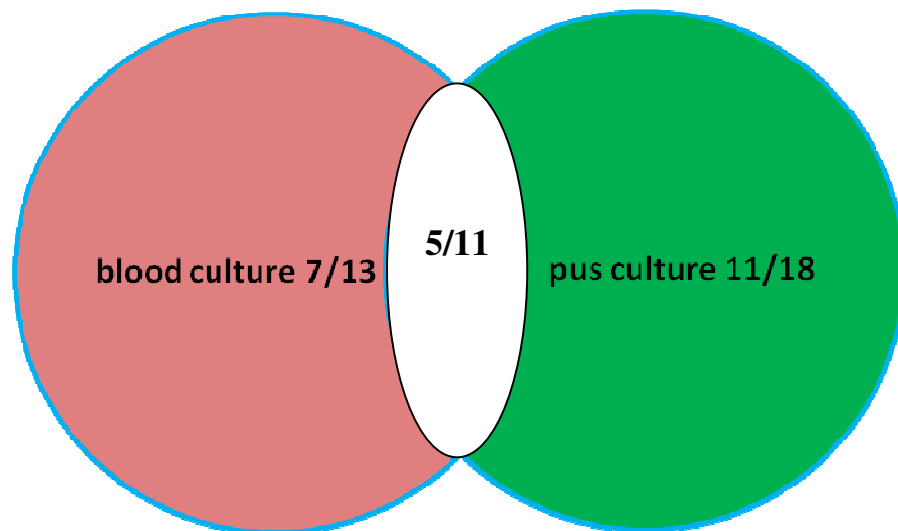
Table 7

Pattern of organism isolated during removal

Organism	Blood culture	Pus/Catheter tip Culture
Candida*	5	2
Aspergillus*	1	1
Staphylococcus aureus**	-	2
MRSA **	2	2
Coagulase negative**	2	4
Enterococcus**	1	1
Enterobacter***	0	2
Pseudomonas***	1	1
Gram negative bacilli***	2	4
Contaminants	1	-
No growth	9	10
Not done	77	72
Total	101	101

* Fungal organisms *** Gram negative organisms ** Gram positive organism

Figure 12 Cultures at removal



Out of 101 children, 29 children had pus/catheter tip culture and 24 children had blood culture done before the chemoport removal. 11 children had both blood culture and pus/catheter tip culture out of which 5 had positive growth. 18 children had only pus/catheter tip culture and 11 had a positive pus/catheter tip culture. 13 children had only blood culture and 7 children had positive blood culture.

Table 8

Pre insertion chemotherapy

Pre insertion chemotherapy	Successful utilization of chemoport	Complications	Total
Yes	122	35* (12)	157
No	43**	15 (5)	58
Total	165	50 (17)	215

Note: Bold figure within brackets under the heading complications denote death

* The neck broke at removal of chemoport after completion of chemotherapy.

** 1 child had sepsis after 6 days the completion of chemotherapy.

24 were excluded from further analysis for the following reasons:

* 14 children were lost to follow up and were excluded from the study.

* 7 children were referred for chemotherapy and were excluded from the study.

* 2 were discharged on request and were excluded from the study.

* 1 child's records could not be accessed as hospital number was not known and excluded from the study.

Chemoport was inserted after the initiation of chemotherapy in 157 children and 58 children had chemoport inserted as soon as the diagnosis was made in 215 children. Out of 157 children who received chemotherapy before insertion, 122(77.70%) had completed or were still going on with chemotherapy and 35 (22.30%) had complications including death. 43 (74.1%) children completed chemotherapy or were undergoing chemotherapy and 15 (25.9%) children had complications including death out of 58 children who did not receive chemotherapy before insertion. Odd's ratio was **1.04** (confidence interval between 0.8-1.2) with P value 0.58.

Table 9

Seniority of the surgeon

Seniority	Successful utilization of chemoport	Complicated inclusive of death with chemoport in situ	Total
Consultant	60*	26** (7)	86
Registrar	98	21 (9)	119
Not known	7	3 (1)	10
Total	165	50 (17)	215

Note: Bold figure within brackets under the heading complications denote death

* 1 child developed sepsis after the completion of chemotherapy.

** Neck broken during the chemoport removal on table.

All the chemoport insertion were done with consultant having scrubbed on the case. Out of 215 children, the primary surgeon in 86 was consultant (assistant professor and above), 119 was registrar and 10 were unknown as the theatre details were not available.

60 (69.8%) children were in the completed and going on group and 26 (30.2%) were in the complicated which included death out of the 86 insertions done by consultants. 98 (82.4%) were in the completed and going on group and 21 (17.6%) were in the complicated which included death out of the 119 insertions done by registrars. 7 (70%) were in the completed and going on group and 3 (30%) were in the complicated group out of the 8 for which operator was unknown. P value was calculated as 0.09 by chi square test.

Table 10

Duration of surgery

Duration of surgery Min	Successful utilisation of the port	Complicated inclusive of death with chemoport in situ	Total
<60	4	1	5
60-120	136	35* (14)	171
>120	23**	13 (3)	36
Not known	2	1	3
Total	165	50 (17)	215

Note: Bold figure within brackets under the heading complications denote death

* Neck broken during the chemoport removal on table.

** 1 child developed sepsis after the completion of chemotherapy.

The median duration for the insertions was 100 min. Out of 215 children, 5 were less than 60 min, 171 were done between 60-120min, 36 were done in more than 120min and 3 were unknown as the theatre details were not available. There were no operative complications in the entire series. P value was calculated as 0.23 by chi square test.

Table 11

Serum albumin at insertion

Serum albumin at insertion g/dl	Successful utilization of chemoport	Complicated inclusive of death with chemoport in situ	Total
<3.5	14*	3 (1)	17
3.5-5.0	72	21 (6)	93
>5.0	3	1	4
Not known	76	25** (10)	101
Total	165	50 (17)	215

Note: Bold figure within brackets under the heading complications denote death

* 1 child developed sepsis after the completion of chemotherapy.

** Neck broken during the chemoport removal on table.

Serum albumin was studied as a nutritional marker. P value was calculated as 0.92 by chi square test. Serum albumin did not show any statistical significance with the complications.

Table 12

Prothrombin time (PT) at insertion

PT at insertion sec	Successful utilization of chemoport	Complicated inclusive of death with chemoport in situ	Total
<10	6	2 (1)	8
10-12.5	86	24* (9)	110
>12.5	22**	8 (2)	30
Not done	51	16 (5)	67
Total	165	50 (17)	215

Note: Bold figure within brackets under the heading complications denote death

* Neck broken during the chemoport removal on table.

** 1 child developed sepsis after the completion of chemotherapy.

PT was studied as a risk factor for complications. P value was calculated as 0.95 by chi square test. PT was not statistically significant.

Table 13

INR at insertion

INR	Successful utilization of chemoport	Complicated inclusive of death with chemoport in situ	Total
<1	35	10 (4)	45
1-1.25	73	22* (8)	95
>1.25	6**	2	8
Not done	51	16 (5)	67
Total	165	50 (17)	215

Note: Bold figure within brackets under the heading complications denote death

* 1 child developed sepsis after the completion of chemotherapy.

** Neck broken during the chemoport removal on table.

INR was studied as a risk factor for complications. P value was calculated as 0.997. INR was not statistically significant.

Table 14

Platelets at insertion

Platelets lakh/cumm	Successful utilization of chemoport	Complicated inclusive of death with chemoport in situ	Total
< 50000	65 *	21** (8)	86
50000-100000	19	6 (4)	25
>100000	81	23 (5)	104
Total	165	50 (17)	215

Note: Bold figure within brackets under the heading complications denote death.

* 1 child developed sepsis after the completion of chemotherapy.

** Neck broken during the chemoport removal on table.

Platelet count was studied as a risk factor for complications. P value was calculated as 0.92 by chi square test. Platelets were not statistically significant.

Table 15

Total count at insertion

Total count Cells/cumm	Successful utilisation of chemoport	Complicated inclusive of death with chemoport in situ	Total
<4000	71	20 (6)	91
4000-10000	54	15* (8)	69
>10000	41**	14 (3)	55
Total	165	50 (17)	215

Note: Bold figure within brackets under the heading complications denote death

* Neck broken during the chemoport removal on table.

** 1 child developed sepsis after the completion of chemotherapy.

Out of 215 insertions, 71 were successfully using their chemoport despite the total count being less than 4000 cells/cumm at insertion. Out of the 91 children with counts <4000 cells/cumm there were 20 complications inclusive of 6 deaths. The number of complications came down as the total count reached the normal values.

P value was calculated as 0.86 by chi square test.

Table 16

Absolute neutrophil count (ANC) at insertion

ANC cells/microlitre	Successful utilization of the chemoport	Complicated	Odd's ratio	Total
<500	66*	12 (4)	2.21 (1.03-5.0)	78
500-1000	13	11** (4)	1.13 (0.5-2.25)	24
1000-1500	11***	4 (2)	1.07 (0.5-2.13)	15
1500-2000	11	4 (2)	1.01 (0.4-2.05)	15
>2000	62	19 (5)	-	81
Total	165	50 (17)	-	215

Note: Bold figure within brackets under the heading complications denote death

*2 children differential counts could not be done as the total counts was less than 500.

** Neck broken during the chemoport removal on table.

*** 1 child developed sepsis after the completion of chemotherapy.

Complications seems to be decreasing with increasing ANC more than 500 cells/microlitre. P value was calculated as 0.03 by chi square test.

Odd's ratio was calculated at each level by merging the cells beyond each level. Odd's ratio was 2.21 (confidence interval between 1.03-5.0 with a P value of 0.02) for ANC < 500 cells/microlitre. Odd's ratio was statistically significant at ANC <500 cells/microlitre at insertion. However, the Odd's ratios beyond the ANC level of 500 cells/microlitre were not significant.

Table 17

Absolute neutrophil count (ANC) at removal

ANC Cells/microlitre	Completed	Complicated	Total
<500	14*	21	35
500-1000	2	1	3
1000-1500	7	3	10
1500-2000	4	1	5
>2000(normal)	42	6**	48
Total	69	32	101

*1 child had sepsis after completion of chemotherapy.

** 1 had neck broken at the time of chemoport removal.

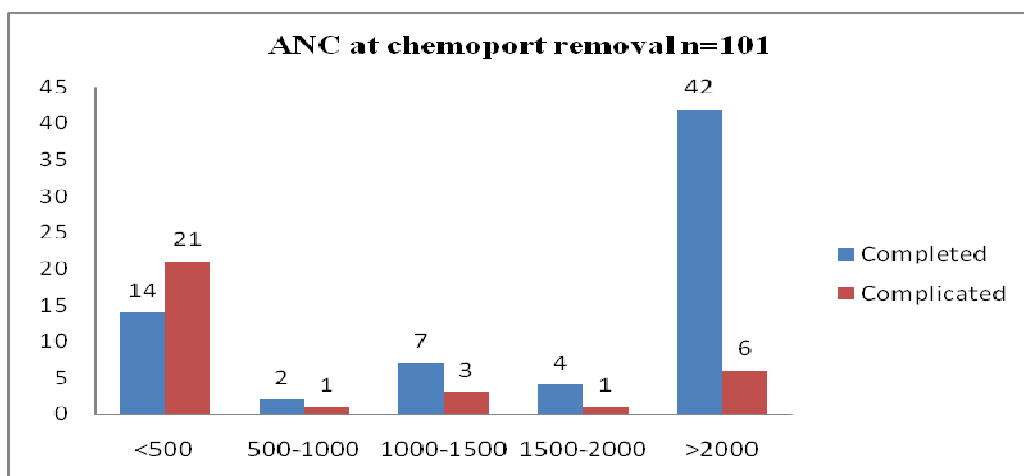


Table 17(a)

ANC at removal with complications

ANC	Infection	Sepsis	Haemotoma	Thrombo sis	Extrav asatio	Discontinue d treatment	Total
<500	17	-	1	2	1	-	21
500- 1000	1	-	-	-	-	-	1
1000- 1500	2	-	-	-	-	1	2
1500- 2000	1	-	-	-	-	-	1
>2000	4	1	-	1	-	1	7
Total	25	1	1	3	1	1	32

There were totally 101 removals out of the 239 chemoport insertions. Most of these removals had complications which occurred at ANC <500 cells/microlitre.

Table 18

Total Count (TC) at removal

TC cells/cumm	Completed	Complicated	Total
<4000	23*	27	50
4000-10000	42	3	45
>10000	4**	2	6
Total	69	32	101

* 1 child had sepsis after completion of chemotherapy.

** 1 child had neck broken during chemoport removal after completion of chemotherapy.

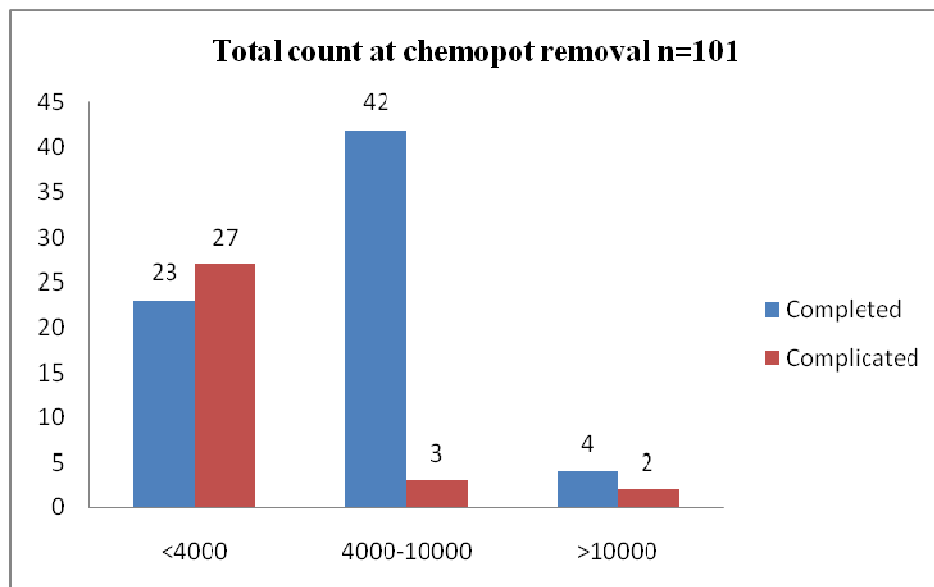


Table 18(a)

TC at removal with complications

TC	Infection	Sepsis	Hematoma	Thrombosis	Extravasation	Discontinued treatment	Total
<4000	21	-	1	3	1	1	27
4000- 10000	2	1	-	-	-	-	3
>10000	2	-	-	-	-	-	2
Total	25	1	1	3	1	1	32

Most of the complications occurred at TC <4000 cells/cumm.

Table 19

Platelets at removal

Platelets lakh/cumm	Completed	Complicated	Total
<50000	9	15	24
50000-1lakh	2	6	8
>1lakh	58*	11	69
Total	69	32	101

* 1 child had sepsis after completion of chemotherapy and 1 had neck broken at the time of chemoport removal.

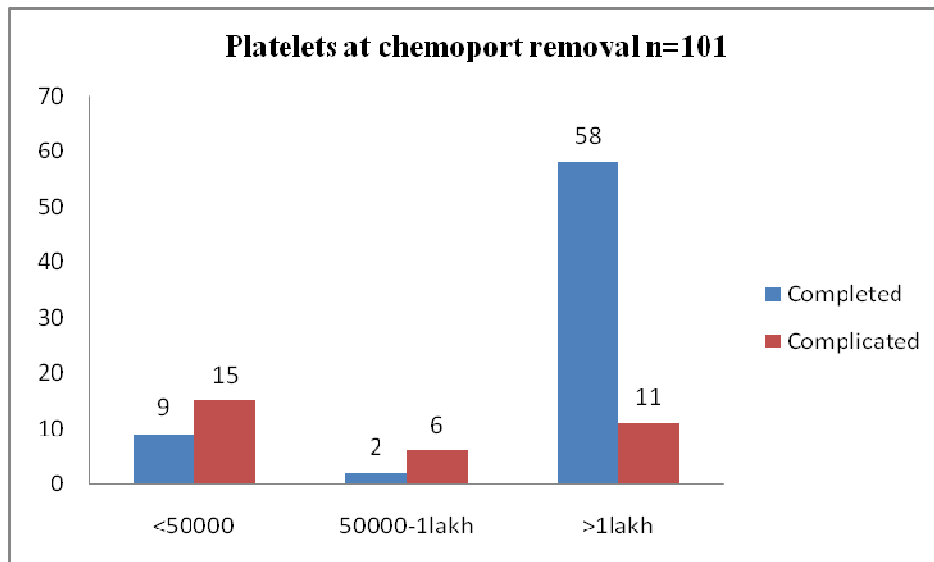


Table 19(a)

Platelets at removal with complications

Platelet count	Infection	Sepsis	Hematoma	Thrombosis	Extravasation	Discontinuation of treatment	Total
<50000	13	-	1	1	-	-	15
50000-1 lakh	4	1	-	1	-	-	6
>1 lakh	8	-	-	1	1	1	11
Total	25	1	1	3	1	1	32

Infection was most common complication in platelets <50000 cells/cumm and only one child had a hematoma with platelets <50000cells/cumm.

Table 20

In situ period of chemoport associated with complications

Duration	Infection	Sepsis	Thrombosis	Hematoma	Extravasation	Total
<6 weeks	6	-	1	1	-	8
>6 weeks	19	1	2	-	1	23
Total	25	1	3	1	1	31

6 weeks duration was taken as the cut off for early and late complications with the premise that complications occurring within 6 weeks would be related to the surgical procedure.

Out of 31 complications for which chemoport were removed, 8 complications were seen in < 6 weeks and 23 complications were seen in > 6 weeks duration with chemoport. 6 children had infection, 1 had thrombosis and 1 had hematoma within 6 weeks as the complication leading to removal of the port out of 31 children who had complications. 23 children had complications after 6 weeks. Infection was the most common complication during both time periods.

DISCUSSION

The vascular access in paediatric oncology patients is required for a long duration and hence chemoports are used. In this study, we retrospectively studied the utilisation of chemoport and the associated morbidity in our centre. We also tried to identify the significant risk factors responsible for complications which resulted in the removal of the chemoport. This was done in order to draw the guidelines for best medical practice with respect to chemoports for our institution.

There were a total of 239 chemoport insertions and 101 removals from January 2007 to December 2013 in paediatric cohort at our centre. Most of the children were in the age group of 1-6 years constituting to about 59% (age range 21 days to 17 years) of the total insertions. There has been a steady increase in the number of chemoport insertions from 2007 to 2013 reflecting an increasing acceptability of the chemoports amongst the paediatric oncological patients. **Currently, between 50 and 60 chemoports are inserted every year.**

Most of the children who had chemoport insertions had **lymphoproliferative disorders mainly leukemias accounting for 172 (72%)** out of 239 children. The solid tumours comprised the rest and the most common were bone tumours and neuroblastoma.

The longest duration for which the chemoport was in situ was 1461 days and shortest was 2 days (Child was lost to follow up). **The median duration of the chemoport remaining in situ in those who successfully completed chemotherapy was 411.5 days.** Children with AML, ALL require intensive chemotherapy for atleast 6

months. Hence, chemoport was inserted for the long term administration of chemotherapy.

The indications for the removal (101 children) of the port in our cohort were completed chemotherapy (67%), infection (26%), thrombosis (3%), extravasation (1%), hematoma (1%), broken catheter (1%) and discontinued treatment (1%) as the tumour was resistant to chemotherapy. In this study, the most common indication for the removal of chemoport was completion of the chemotherapy.

Complications resulted in the removal of chemoports before completion of the chemotherapy in 32 children accounting for 31.7% of the removals. The most common complication which lead to removal of the port was infection seen in 26 patients. Local infection defined as induration, erythema, discharge and tenderness was seen in 42.4%, sepsis was seen in 34.6% and 23% were having local infection and sepsis at the time of removal.

60% were able to complete the chemotherapy or were undergoing chemotherapy with a positive culture before insertion and 79.77% were able to complete or were undergoing chemotherapy in the group of culture negative patients. Odd's ratio was calculated to be 0.75 with a P value of 0.29 and found to be statistically insignificant.

In our study, the most common isolate on blood culture was candida seen in 5 out of 29 patients and coagulase negative staphylococci and gram negative bacilli were the most common organism on pus/catheter tip culture seen in 4 out of the 32 chemoport removals which were removed for various complications. Other organisms were MRSA, enterobacter, enterococcus, pseudomonas, staphylococcus and aspergillus species.

Overall, various staphylococci including MRSA was the most common isolate in those with infection.

An attempt was made to identify the risk factors resulting in the complications that lead to the removal of the port. The risk factors studied were pre insertion chemotherapy, duration of surgery, seniority of the surgeon, serum albumin, PT, INR, platelet count, total count and absolute neutrophil count.

Table 21 Odd's ratio and P value for risk factors studied

Risk factor	Odd's ratio/Chi square value	P value
Pre insertion chemotherapy	1.04 (0.8-1.2)*	0.58
Seniority of the surgeon	4.6978**	0.09
Duration of surgery	4.2785**	0.23
Serum albumin at insertion	0.457**	0.92
Prothrombin time at insertion	0.3512**	0.95
INR	0.0557**	0.997
Platelet count at insertion	0.1487**	0.92
Total count at insertion	0.2993**	0.86
Absolute neutrophil count <500 cells/cumm at insertion	2.21 (1.03-5.0)*	0.02

* Odd's ratio

** chi square value

The significant risk factor identified was absolute neutrophil count (ANC). It seemed to support the hypothesis that as immunity fell, propensity for infection increases. On studying various levels of absolute neutrophil count, it was noted that a statistically significant rise in complication was present with absolute neutrophil count <500 cells/microlitre.

Table 22

Odd's ratio at various levels for absolute neutrophil count (ANC)

ANC cells/microlitre	Successful utilization of the chemoport	Complicated	Odd's ratio	Total
<500	66*	12 (4)	2.21 (1.03-5.0)	78
500-1000	13	11** (4)	1.13 (0.5-2.25)	24
1000-1500	11***	4 (2)	1.07 (0.5-2.13)	15
1500-2000	11	4 (2)	1.01 (0.4-2.05)	15
>2000	62	19 (5)	-	81
Total	165	50 (17)	-	215

Moreover, this table seems to suggest a dose related inverse relationship between ANC and complication. However, statistical significance could not be demonstrated at each level.

ANC dropping during chemotherapy was also associated with greater risk of complications. 21 out of 32 (65%) children had complications with ANC <500 cells/microlitre. All these seem to suggest that neutropenia precludes longevity of the chemoport remaining in situ.

It is of interest that children with thrombocytopenia <50000 cells/cumm in our cohort had more complications. However, there were only 4 thrombotic and hemorrhagic complications noted in the entire 32 children with complication which lead to chemoport removal (1 thrombotic and 1 hematoma in <50000 cells/cumm). The neutropenia and thrombocytopenia seemed to point myelosuppression as the common culprit.

Complications were studied with respect to time of occurrence since insertion. A time period of 6 weeks following insertion was chosen to identify surgery related complications. The most common complication which occurred at a duration of < 6 weeks from the time since insertion of the port was infection seen 6 out of the 8 patients. The other complications seen were thrombosis in 1 child and hematoma in the other.

The most common complication which occurred after 6 weeks following the insertion of the chemoport was infection seen in 20 out of the 23 children. Other complications which were seen after 6 weeks of insertion of the chemoport were thrombosis in 2 children and extravasation in one. Most complications occurred after 6 weeks.

CONCLUSION

- Chemoport is a good tool for vascular access in cancer requiring long term chemotherapy.
- Chemoports are not without complications. The most common complications are infectious complications amounting to 10.87%.
- Absolute neutrophil count <500 cells/microlitre is a strong predictor of complications with chemoport at any stage of chemotherapy.
- The common isolates are staphylococci and fungi and appropriate empiric antibiotics depending on the local sensitivity pattern should be employed in sepsis.
- Surgical complications were minimal and not related to the Seniority of the primary surgeon or duration of surgery in our cohort.
- With proper maintenance and care of the port, it can be used safely as a vascular portal for administration of chemotherapy for prolonged periods of time.

RECOMMENDATIONS

- Absolute neutrophil count seems to be a contraindication for the insertion of chemoport.
- Efforts to maintain absolute neutrophil count >500 cells needs to be studied and employed in the clinical setting.

References:

- 1) Andrassy RJ, Hays DM. General Principles of surgery. Chapter 10. Principles and Practice of Paediatric Oncology. 3rd edn. Pizzo PA, Poplock DG. Lippincott-Raven Publishers. Philadelphia.1997:275-9.
- 2) Howritz JR, Lally KP. Vascular Access Chapter 8. Paediatric Surgical Oncology. Andrassy RJ. W.B. Saunders company. Philadelphia.:137-48.
- 3) Bishop L, Dougherty L, Bodenham A, Mansi J, Crowe P, Shannon M et al. Guidelines on the insertion and management of central venous access devices in adults. International journal of Laboratory hematology. 2007;29:261-78.
- 4) [http://en.wikipedia.org/wiki/Port_\(medical\)](http://en.wikipedia.org/wiki/Port_(medical)).
- 5) Kanter RK, Zimmerman JJ, Strauss RH, Stoeckel KA. Central venous catheter insertion by femoral vein. Safety and effectiveness for the pediatric patient. Paediatrics.1986;77(6):842-7.
- 6) Fonkalsurd EW, Berquist W, Burke M, Ament ME. Long term hyperalimentation through saphenous femoral venous catheterization. Am J sur.1982;143:209-11.
- 7) Donahoe PK, Kim SH. The inferior epigastric as an alternative site for central venous hyperalimentation. J Paediatr Surg.1980;12:737-8.
- 8) Azizkhan RG, Taylor LA, Jacques PF, Mauro MA, Lacey SR. Percutaneous translumbar and transhepatic inferior venacaval catheters for prolonged venous access in children. J Paediatr Surg.1992;27:165-9.

- 9) Robertson LJ, Jacques PF, Mauro MA, Azizkhan RG, Robards J. Percutaneous inferior vena cava placement of tunneled silastic catheters for prolonged vascular access in infants. *J Paediatr Surg.*1990;25:596-8.
- 10) Newman BM, Cooney DR, Karp MP, Jewett TC Jr. The intercostals vein: An alternative route for central venous alimentation. *J Paediatr Surg.*1983.732-3.
- 11) Silverman SH, Stringel G. Two techniques for central catheter placement in the hypogastric and azygous vein. *Paediatric surgery International.*1988;3:62-3.
- 12)<http://www.atlasofpelvicsurgery.com/10MalignantDisease/2SubclavianPort-A-Cath/cha10sec2.html>.
- 13) Nam SH, Kim DY, kim SC. Complications and risk factors of infection in paediatric Hemato-oncology patients with Totally implantable access ports (TIAPs). *Paediatric Blood Cancer.* 2010;54:549
- 14) Krasna IH, Krause T. Life threatening fluid extravasation of central venous catheters. *J pediater surg.*1991;26:1346-8.
- 15) Ross P Jr, Seashore JH. Bilateral hydrothorax complicating central venous catheterization in a child. *J Pediatr Surg.*1989:263-4.
- 16) Agarwal KC, Ali khan MA, Falla A, Amato JJ. Cardiac perforation from central venous catheters: Survival after cardiac tamponade in an infant.1984;73:333-8.
- 17) Groegor SJ, Lucas AB, Thaler HT, Klar HM, Brown AE, Kiehn TE et al. Infectious morbidity Associated with Long term use of venous access devices in Patients with cancer. *Ann Intern Med* 1993;119(12):1168-74.

- 18) Wiener ES, McGurie P, Stolar CJH et al. The CCSG prospective study of venous access devices: An analysis of insertions and causes for removal. *J Paediatr Surg.*1992;27:163-4.
- 19) Raucher HS, Hyatt AC, Barzilai A et al. Quantitative blood cultures in the evaluation of septicaemia in children with Broviac catheters. *J pediatr.*1984;104(1):29-33.
- 20) Hiemenz J, Skelton J, Pizzo PA. Perspective on the management of catheter related infections in cancer patients.1986;5:6-11.
- 21) Nahata MC, King DR, Powell DA, Marx SM, Ginn-Pease ME. Management of catheter related infections in cancer patients. *JPEN.*1988;12:58-9.
- 22) Trooskin SZ, Donetz AP, Harvey RA, Greco RS. Prevention of catheter sepsis by antibiotic bonding. *Surgery.*1985;97:547-51.
- 23) Bjornson HS, Colley R, Bower RH, Duty VP, Schwartz-Fulton JT. Association between microorganisms growth at the catheter insertion site and colonization of the catheter in patients receiving total parenteral nutrition, *Surgery.*1982;92:720-7.
- 24) Jones GR, Konsler GK, Dunaway RP, Lacey SR, Azizkhan RG. Prospective analysis of urokinase in the catheter related sepsis in pediatric hematology-oncology patients. *J Pediatr Surg.*Mar 1993;28:355-7.
- 25) Dato VM, Dajani AS. Candidemia in children with central venous catheters. Role of catheter removal and amphotericin B therapy. *Pediatr Infect Dis J.*1990;9:309-14.
- 26) Rotrosen D, Gibson TR, Edwards JE Jr. Adherence of candida species to intravenous catheters. *The journal of infectious diseases.* Mar 1983;147(3):594.

- 27) Shulman RJ, Reed T, Pitre D, Laine L. Use of hydrochloric acid to clear obstructed central venous catheters. JPEN.1988;12:509-10.
- 28) Winthrop AL, Wesson DE. Urokinase in the treatment of occluded central venous catheter in children. J Pediatr Surg.1984;19:534-38.
- 29) Aitken DR, minton JP. The “pinch-off sign”: A warning of impending problems with permanent subclavian catheters. Am J Surg.1984;148:633-6.
- 30) Hassal E, Ulich T, Ament ME. Pulmonary embolus and Malassezia pulmonary infection related to urokinase therapy. J Pediatr.1983;102:722-5.
- 31) Mittal L, Kalra M and Mahajan A. Acceptability of Subcutaneous Implantable Ports (SIPs) in Cancer Patients. The Indian journal of Paediatrics Dec2012;79;12:1601-04.
- 32) <http://www.gain-ni.org/images/Uploads/guidelines/Gain-CVAD-2012.pdf>.
- 33) Pearl JM, Goldstein L, Ciresi KF. Improved methods in long term venous access using the P.A.S. port. Surg Gynecol Obstet.1985;20:725-7.
- 34) Mirro J Jr, Rao BN, Kumar N et al. Comparison of placement techniques of externalized catheters and implantable port use in children with cancer. J Pediatr Surg.1990;25:120-4.
- 35) Ingram J, Weitzman S, Greenberg ML, Parkin P, Filler R. Complications of indwelling venous access lines in the paediatric hematology patients. A prospective comparison of external venous catheters and subcutaneous ports. Am J of Pediatr Hematol Oncol.1991;13:130-6.

PROFORMA FOR THE CHEMOPORT STUDY

Unique identification number

Hospital number

Name

Age

Gender

Oncological diagnosis

Surgical details:

Date of insertion

Seniority of surgeon

Duration of surgery

Investigations at insertion:

PT

Albumin

Platelets

INR

White cell count

ANC

Date of adverse event

Date of removal

Duration of chemoport

Reason for removal

Adverse events- Y/N

If yes Thrombosis, infection, cutaneous site infection, systemic complication-

Investigations at the time of removal for complications-

Total counts

ANC

Blood culture

Catheter tip culture/pus culture

Format for Informed Consent Form for Subjects

Informed Consent form to participate in a research study

Study Title: Utility of chemoport in Paediatric Oncological patients, a surgical perspective

Subject's Initials: _____

Subject's Name: _____

Date of Birth / Age: _____

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions.

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

(v) I agree to take part in the above study.

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: ____/____/____

Signatory's Name: _____

Signature:

Or

Representative: _____

Date: ____/____/____

Signatory's Name: _____

Signature of the Investigator: _____

Date: ____/____/____

Study Investigator's Name: _____

Signature of the Witness: _____

Date: ____/____/____

Name & Address of the Witness: _____

Sl No	Age	Sex	Diagnosis	Indication	Insertion TC	PT insertion	Platelets	Blood cultures	Chemo	Duration port	ANC removal	TC removal	Platelets removal	Blood Cul removal	Pus/Catheter culrem rem	Duration of surgery	Seniority	ANC at insertion	ser alb insertion	Without port	INR insertion
1	2	F	Medulloblastoma	infection	11100	10.5	498000	N	N	102	28	1400	19000	candida	E Coli	1:30(90)	S	3850	4.8	completed	0.97
2	3	M	ALL	infection	39300		72000	N	Y	291	1632	3400	282000	candida	No growth	1:45(105)	S	1556		completed	
3	2	M	ALL	completed	5800		374000	N	N	321	52	1300	117000			1:40(100)	S	1740			
4	1	M	ALL	completed	1500		22000	N	Y	1072	1275	2500	184000		No growth	1:30(90)	S	30	3.9		
5	1	F	Pre B ALL	completed	30800		12000	No growth	Y	1114	6336	9900				2:00(120)	S	567	4.4		
6	3	f	ALL		9200		196000		N	796						1:25(85)	S	3220		death	
7	10	M	ALL	completed	4700		236000	N	N	1432	3104	9700	165000			1:45(105)		1271	4.2		
8	10	F	Osteosarcoma																		
9	3	F	Pre B ALL		1500	10.8	225000	no growth	Y	195						1:40(100)	S	75	4	don't know referred	0.93
10	2	F	Pre B ALL	completed	4200	11.4	344000	N	N	271	Not done	300	71000	Coag nega		2:00(120)	S	1638			1.04
11	12	M	PNET	completed	11800	clot	450000	N	N	319	100	1000	149000	No growth		2:00(120)	S	7080			Clot
12	4	F	PRE B ALL	completed	1500		29000	N	Y	909	1984	3100	316000		No growth	1:50(110)		60			
13	1	F	Pre B ALL	thrombosis	2500		138000	N	Y	34	221	1300	16000			2:00(120)	S	550	3.5	completed	
14	10	M	Leukemia	completed	8200		157000	N	Y	254	5256	7300	359000			2:00(120)	S	2581			
15	2	M	Pre B ALL	completed	1200		22000	N	Y	1074	3150	5000	313000			1:30(90)	S	84	4.9		
16	5	M	Osteosarcoma		13800		342000	N	N	1461						1:50(110)	S	8556	4.2	palliative care	
17	4	F	metastatic neuroblastoma	completed	3800	15.3	485000	N	Y	208	4225	5700				2:15(135)	J	2508			1.23
18	11	M	Osteosarcoma	completed	4500		172000	N	N	308	2760	4600	167000			2:20(140)		2655	4.6		
19	5	M	Pre B ALL		13900	12.8	27000	N	Y	738						1:45(105)	J	1740		don't know	1.02
20	3	M	Pre B ALL	completed	1000	14	8000	No growth	Y	883	3332	4900	312000			1:20(80)	J	120			1.12
21	2	F	metastatic neuroblastoma		7200	13.2	218000	No growth	N	225						2:15(135)	J	8264		don't know	1.15
22	10	M	Ewing's sarcoma		32600		162000	N	N	86						1:45(105)	S	15984		death	
23	2	F	Pre B ALL	infection	3200	10.2	225000	N	N	118	5668	10900	245000	No growth	No growth	2:00(120)	S	1472	4.6	completed	1.03
24	1	M	Medulloblastoma	thrombosis	7000		284000	N	N	332	2300	5000	269000			2:15(135)	S	3481		completed	
25	4	M	RMS OF URINARY BLADDER	infection	11700	10.6	239000	N	N	134	399	2100	177000	candida		2:10(130)	S	6084	6	completed	0.92
26	2	M	Pre B ALL	Completed	2600	12.5	18000	N	Y	674	40	1000	193000	No growth		1:40(100)	S	89			1.08
27	1	F	AML	completed	92500	12.8	44000	N	Y	168	Not done	1800	3000			1:40(100)	J	4274	4.3		1.09
28	2	F	Pre B ALL	neck broken+comp	4400	11.5	34000	No growth	Y	981	5586	14700	292000			1:30(90)	S	623			1
29	6	M	metastatic neuroblastoma	infection	7600	13.4	676000	No growth	N	50	6	600	8000	gram negative		1:25(85)	S	5092		completed	1.16
30	4	F	Pre B ALL	completed	2700	13.8	167000	No growth	Y	510	1568	2800	370000			1:45(105)	J	1809	4.4		1.31
31	4	M	Pre B ALL	Completed	8100	12.3	354000	N	N	1129	4656	9700	190000			1:35(95)	J	3969			1.07
32	4	M	Pre B ALL	completed	1600	12.6	11000	No growth	Y	1007	2160	5400	244000			1:40(100)	S	32			1.1

33	4	F	Pre B ALL	infection	2000		10000	candida tropicalis	Y	75	10	500	31000	candida		2:15(135)	S	576	2.5	completed	
34	6	M	Pre B ALL	completed	2600	11.6	8000	No growth	Y	1171	2950	5900	268000			1:45(105)	S	130	4		1.01
35	14	M	Osteosarcoma	completed+sepsis	16800	15.5	767000	No growth	N	225	490	1400	105000	enterococcus		2:10(130)	S	13776	1.3		1.38
36	2	F	Pre B ALL	completed	3900	12.4	89000	No growth	Y	1071	5040	8400	307000			2:15(135)	S	1755	3.7		1.13
37	4	M	Pre B ALL	Completed	3600	9.9	29000	No growth	Y	952	3080	4000	188000			2:05(125)		936	4.3		0.92
38	6 month	M	Pre B ALL	infection	1900	11.2	56000	N	Y	265	not done	200	189000		Enterobacter R	2:30(150)	S	342	3.7	completed	1.02
39	5	M	Pre B ALL	completed	1300	9.9	7000	No growth	Y	524	2107	4300	150000			1:45(105)	S	13			0.92
40	9	F	AML	infection	1500	13	11000	No growth	Y	80	Not done	200	9000	E coli	E Coli	1:40(100)		15	4	completed	1.22
41	2	M	Pre B ALL	Completed	4600	11.9	35000	N	Y	1180	4272	4600	203000			2:00(120)	S	230	4.2		1.03
42	4	M	Pre B ALL	Completed	22800	11.2	21000	No growth	Y	980	4060	7100	156000			1:50(110)		4799	3.2		1.05
43	3 month	F	PNET		8900	10.7	762000	contaminants	N	186						1:00(60)		3738		death	0.97
44	4	F	Pre B ALL	completed	3800	11.3	156000	N	Y	917	1092	2600	216000			1:30(90)	S	1216	5		1.02
45	10	F	AML		5300	9.2	21000	No growth	Y	28						1:15(75)	S	636	4.1	death	0.86
46	1	M	Pre B ALL		6800	10.5	27000	No growth	Y	4						2:20(140)	S	204	4.1	don't know referred	0.97
47	2	M	Pre B ALL	infection	7400	10.4	363000	No growth	N	206	30	1000	161000		Staph. Aureus S	1:50(110)	S	1776	4.2	completed	0.97
48	2	F	Pre B ALL	completed	5100	13	51000	No growth	Y	276	2482	3400	384000			2:15(135)	S	771			1.22
49	13	F	lymphoma		7200	13.2	218000	No growth	N	717						1:45(105)	S	6264		don't know	1.15
50	12	F	AML	completed	5000	13.1	42000	No growth	Y	203	2750	5000	217000			1:55(115)	S	224			1.22
51	3	F	AML	hematoma	3700	11.8	12000	N	Y	14	10	500	4000			1:50(110)	S	740		death on 28/03/2011	1.1
52	3	M	AML	infection	11900	9.8	363000	N	N	199	Not done	200	11000		enterobacter	1:45(105)	S	2975	4.5	death on 13/09/2011	0.88
53	2	F	AML	completed	65300	11.5	197000	N	Y	159	56	800	85000		No growth	1:30(90)	S	4963	2.9		1.06
54	13	M	AML		36000		18000	N	Y	349						1:50(110)	S	18360	4.4	completed	
55	8month	M	Neuroblastoma	completed	15400		713000	No growth	N	183	2640	5500	234000			1:35(95)	S	12012	4.6		
56	2	M	ALL	completed	28200	10.8	82000	No growth	Y	637	4557	9300	328000		Coagulase neg			1574			0.93
57	2	M	clear cell sarcoma R kidney	completed	11800		337000	N	N	245	352	2200	180000			2:15(135)	S	3540			
58	15	F	Hodgkin lymphoma	completed	14800	12	410000	No growth	N	652	2475	5500	192000			1:50(110)	S	13172	3.2		1.09
59	1	F	LCH X	completed	9000	9.3	315000	No growth	N	477	6760	8700	360000		Enterococcus	2:05(125)	J	5220			0.87
60	6	F	ALL		4600	11.3	54000	No growth	Y	949						2:20(140)	S	743		still going on	1.02
61	6	F	ALL		10700	10.8	22000	No growth	Y	950						1:20(80)	S	163		still going on	0.93
62	7	M	ALL		1000	10.2	59000	N	Y	950						1:15(75)	S	60		still going on	0.95
63	2	M	Acute Leukemia	completed	15000	12.4	46000	N	Y	140	18	900	14000			1:45(105)	J	2414			1.13
64	5	M	Pre B ALL		2400	11.5	26000	No growth	Y	851						1:40(100)		145		still going on	1.06
65	13	F	ALI		4600	10.4	56000	No growth	Y	54						2:05(125)	S	1556	4.1	death	0.97
66	3	M	T cell ALL	infection	3100	18.6	424000	No growth	Y	403	1364	3100	396000		Pseudomonas	1:45(105)		776	4.6	don't know	1.72

67	3	M	Neuroblastoma		9500	11.1	469000	No growth	N	566						1:30(90)	S	3705		don't know	1.01
68	2	M	ALL	completed	1100	11	10000	No growth	Y	201	56	2800	9000		No growth	1:50(110)	S	23	4.4		1
69	4	M	Lymphoma	completed	8100		499000	N	N	328	2409	7300	324000			1:30(90)	S	4374			
70	1	f	metastatic neuroblastoma		10700	11.1	471000	No growth	Y	752							S	6099	4.8	dint complete	1.01
71	2	M	Pre B ALL		1200		24000	No growth	Y	226						1:15(75)	S	12		death	
72	1	F	ALL		2100	10	19000	No growth	Y	810						1:05(65)	S	105	3.5	still going on	0.93
73	1	F	ALL		1600	10.5	88000	No growth	Y	810						2:00(120)	S	226		still going on	0.97
74	7	M	Pre B ALL		3300	11.7	18000	No growth	Y	167						1:05(65)	J	627		death	1.06
75	6month	M	Hepatoblastoma		13900		887000	N	N	7						1:45(105)	J	5282	4	don't know	
76	3	M	ALL		22800	9.8	49000	No growth	Y	1055						2:10(130)	S	16416		still going on	0.88
77	8	M	Hepatoblastoma	completed	7800	10.3	305000	N	N	511	4142	10900	32500			1:45(105)	S	2730			0.96
78	8	M	ALL		4000	10.5	367000	N	N	524						1:20(80)	S	1280	4.7	don't know	0.97
79	3	M	Pre B ALL		2500		174000	No growth	Y	1042						2:15(135)	J	1625	4.7	still going on	
80	11	M	AML	infection	15900	12.2	13000	N	Y	65	0	400	17000		E Coli	1:45(105)	J	1479		don't know	1.1
81	11month	M	AML	completed	10200	12.1	17000	No growth	Y	442	Not done	100	9000		No growth	1:30(90)	J	408	4.5		1.13
82	11	M	ALL		600	clot	22000	No growth	Y	1000						2:00(120)	J	12	3.2	still going on	Clot
83	7	F	ALL		7900	10.5	93000	N	Y	190						1:50(110)	J	1933	4.1	death	0.97
84	10	M	Burkitts lymphoma		14600	9.8	506000	No growth	N	19							S	14016	3.8	dis on request23/05/11	0.88
85	3	F	neuroblastoma		6200	10.4	295000	No growth	Y	390						1:30(90)	S	3906		don't know	0.97
86	1	F	Pre B ALL		6100	11.4	8000	N	Y	272						1:55(115)	S	748		don't know referred	1.04
87	1	M	Acute leukemia		1900	10.9	28000	No growth	Y	957						1:30(90)	S	76	4.6	still going on	0.99
88	6 month	F	clear cell sarcoma R kidney		28000	13.5	177000	N	N	111						1:00(60)	S	19600	3.7	don't know	1.26
89	9	M	Pre B ALL		1900	10	14000	No growth	Y	958						2:20(140)	S	190		still going on	0.93
90	2	F	Pre B ALL	Completed	4300	11.7	22000	N	Y	795	2867	6100	161000			1:45(105)	S	440			1.06
91	3	M	Leukemia		2200	10.7	35000	N	Y	820						1:15(75)	S	44		still going on	0.97
92	7	M	AML		6300	11.9	24000	No growth	Y	185						1:45(105)	S	252	3.6	don't know	1.03
93	1	M	Pre B ALL	completed	1200	10	22000	No growth	Y	381	2914	9400	396000			1:50(110)	S	84	4.6		0.93
94	3	M	T cell ALL		3000	11.9	227000	No growth	Y	295						1:45(105)	S	570	4.4	don't know	1.06
95	1	M	Rhabdomyosarcoma L testis	infection	8200	10.5	423000	N	N	243	1056	3300	97000		E Coli	1:35(95)	J	2296	4.2	completed	0.97
96	9	F	Pre B ALL		1400		40000	No growth	Y	790						1:30(90)	J	112	4.1	still going on	
97	1	M	Acute Leukemia		38000	12.4	10700	No growth	Y	26						1:55(115)	J	7604	4.9	don't know	1.08
98	9	F	Ewing's sarcoma	completed	4100	11.1	95000	N	Y	197	Not done	300	45000			1:50(110)	J	2460			1.01
99	3	M	Pre B ALL	infection	2700		18000	N	Y	8	460	2000	32000	No growth	Staph. Aureus S	1:55(115)	S	55		don't know	
100	4	F	AML	Completed	2900		146000	contaminants	Y	539	1564	2600	280000			1:40(100)	S	551	4.1		

101	10	M	ALL		6700	12.4	23000	No growth	Y	194						1:30(90)	J	1216		death	1.13
102	10	F	Osteosarcoma		2700		309000	No growth	Y	734						1:30(90)	J	378		still going on	
103	8	M	Burkitts lymphoma	completed	9900		751000	No growth	N	119	4472	8600	357000			1:35(95)	S	7524			
104	3	F	Pre B ALL		2600		150000	No growth	Y	722						1:45(105)	S	1534	4.3	still going on	
105	6	F	ALL		2800	11.9	41000	No growth	Y	722						2:00(120)	J	281	4.3	still going on	1.03
106	1	m	r Lung GCT	completed	4200	10.9	267000	No growth	N	237	1235	6500	216000			2:00(120)	S	1386			0.99
107	12	F	Pre B ALL		2600	11	493000	N	N	243						2:05(125)	J	1066	4.1	death	1
108	4	F	Pre B ALL		5300	9.4	157000	N	N	680						1:21(81)	J	2703	4.5	still going on	0.92
109	4	M	Pre B ALL		1800	11.8	64000	No growth	Y	652						1:45(105)	J	18		still going on	1.1
110	2	F	Pre B ALL	infection	2700		217000	N	Y	441	4028	5300	408000	staph Coag neg	Staph Coag neg	2:00(120)	J	945		don't know	
111	4	F	Pre B ALL		1900	9.9	88000	N	Y	608						1:35(95)	J	190	4.5	still going on	0.9
112	12	M	Osteosarcoma	completed	18200		491000	N	N	217	494	2600	31000			1:45(105)	J	12922			
113	9	M	Osteosarcoma	infection	11600	11.4	441000	N	N	77	30	1500	35000		candida tropicalis	0:55(55)	J	7540		completed	1.04
114	2	F	Pre B ALL	infection	4500	11.9	17000	No growth	Y	246	48	1600	331000	candida	candida tropicalis	2:00(120)	S	360		completed	1.03
115	2	M	Hepatoblastoma	dint complete	12700		351000	N	N	106	1344	3200	203000			2:00(120)	S	7620	4.1		
116	2	F	Osteosarcoma	Completed	7100		439000	N	N	512	3726	5400	225000			1:30(90)	S	2343			
117	2	F	Pre B ALL		1300		66000	N	Y	423						1:25(85)	S	169		still going on	
118	2	F	Leukemia		3200	11	53000	N	Y	35						2:00(120)	S	704		death	1
119	5	M	Leukemia		1500	12.2	31000	No growth	Y	45						1:25(85)	S	150	3.5	don't know	1.1
120	2	M	Pre B ALL		2600		28000	N	Y	518						1:20(80)	S	286	4.8	still going on	
121	8	F	Medulloblastoma	completed	2800	11.2	355000	N	Y	499	2115	4500	248000			1:25(85)	S	2184			1.05
122	14	M	ALL		4300		179000	N	N	510						1:40(100)	S	1462	4.7	still going on	
123	17	F	Osteosarcoma	completed	7400		230000	N	N	203	1116	3100	147000			1:30(90)	S	4588			
124	6	M	Pre B ALL		5200		311000	No growth	N	496						1:35(95)	J	2240	4	still going on	
125	4	M	Pre B ALL		8100		43000	No growth	Y	469						1:10(70)	J	32	1.5	still going on	
126	13	F	Pre B ALL	infection	4600		43000	contaminants	Y	27	27	900	51000	pseudomonas		1:10(70)	J	2622		don't know	
127	7	M	T cell ALL		4200	11.1	475000	No growth	N	11						0:40(40)	J	3486	3.2	don't know	1.02
128	13	F	Hodgkin lymphoma		9600	10.7	295000	No growth	N	451						1:30(90)	J	7296	2.6	don't know referred	0.97
129	2	M	Pre B ALL		3100	10.8	150000	No growth	Y	440						1:15(75)	J	775	3.9	still going on	0.93
130	6	F	Leukemia		5200		242000	N	N	114						1:15(75)	S	3016	4.6	death	
131	5	M	Leukemia	infection	1300	10.6	20000	No growth	Y	27	2726	2900	95000		No growth	1:30(90)	S	260		don't know	0.92
132	3	M	AML		15300	13	13000	No growth	Y	21						1:30(90)	J	612	2.6	death	1.22
133	7	M	Pre B ALL		1100	12.1	68000	No growth	Y	413						1:30(90)	J	33	4	still going on	1.13
134	12	M	Pre B ALL		2800	10.9	26000	No growth	Y	413						1:25(85)	J	756	3.8	still going on	0.99

135	10	F	PNET		6400		228000	N	N	398						1:45(105)	J	3008	4.2	still going on	
136	7	M	Pre B ALL		2600	12.4	13000	No growth	Y	7						1:45(105)	J	79	3.9	death	1.13
137	11	M	T cell ALL		500	10.2	16000	No growth	Y	398						1:50(110)	J	N		still going on	0.95
138	1	M	AML	completed	6000		452000	N	Y	287	1162	8300	288000	No growth		1:55(115)	J	2580	4.4		
139	3	M	ALL	completed	5500	10.8	333000	No growth	N	273	2376	3600	199000	No growth		1:20(80)	J	1430	4.2		0.93
140	9	M	Neuroblastoma	thrombosis	6000	11.6	319000	No growth	Y	280	24	800	87000	No growth		1:20(80)	J	2280	4	completed	1.01
141	9month	F	ALL		3400		8000	No growth	Y	726						1:10(70)	J	102	3.6	still going on	
142	10	M	Osteosarcoma	completed	2000		205000	No growth	Y	454	3528	7200	206000			1:55(115)	J	40			
143	7	F	ALL		1600	11.9	65000	No growth	Y	713						1:40(100)	J	704		still going on	1.06
144	1	M	ALL		1600	11	63000	No growth	Y	698						1:25(85)	J	32	5.1	still going on	1
145	1	F	Neuroblastoma	completed	13400	10.7	429000	N	N	77	1680	4800	147000			1:45(105)	J	5330	5.2		0.97
146	3	F	Pre B ALL		3400		6000	N	Y	629						1:45(105)	J	35		still going on	
147	6	F	ALL		2000	12.3	8000	No growth	Y	628						1:45(105)	J	22	3.7	still going on	1.07
148	1	M	Neuroblastoma		15700	10	359000	N	N	614						1:40(100)	J	6751	3.7	still going on	0.93
149	6	M	Pre B ALL		3100	11	73000	No growth	Y	600						1:40(100)	J	372		still going on	1
150	5	M	Pre B ALL		5200		425000	No growth	N	600						1:30(90)	J	2704		still going on	
151	5	M	ALL	Extravasation	2200		15000	No growth	Y	476	126	1400	224000	No growth		1:55(115)	J	176		completed	
152	5	M	Embryonal sarcoma-liver	completed	14600	12.5	351000	N	N	365	3630	6600	229000			1:45(105)	J	12410	2		1.08
153	15	F	Osteosarcoma	infection	2100		113000	N	Y	231	8058	10200	63000		Aspergillus		J	105		death on 2/04/2013	
154	10	M	lymphoma		16800	13.2	407000	No growth	N	182						2:00(120)	J	11760		don't know	1.21
155	21days	M	Lymphoma		2100		50000	No growth	Y	46						1:45(105)	J	44		death	
156	6	F	metastatic neuroblastoma		2100	10.5	195000	No growth	Y	490						1:15(75)	J	756		still going on	0.97
157	3	M	ALL		2500		59000	No growth	Y	490						1:30(90)	J	125	4.3	still going on	
158	3	M	Pre B ALL	completed	3400	12.2	21000	N	Y	189	2912	5200	155000	contaminants		1:45(105)	J	374			1.1
159	4	M	AML	completed	15300		38000	N	Y	206	1419	4300	289000			1:40(100)	J	1580			
160	11	M	Lymphoma	Completed	17500	12.4	372000	No growth	Y	336	3710	5300	194000				J	2625	2.8		1.13
161	4	M	metastatic neuroblastoma	completed	8900	11.7	472000	No growth	N	189	8284	10900	244000			1:40(100)	J	5607	2.3		1.06
162	4	M	EMS nasal cavity		3500	11.5	1010000	No growth	Y	431						1:30(90)	J	350		still going on	1.06
163	6	M	metastatic neuroblastoma	Completed	8900	12.4	343000	No growth	N	228	2809	5300	247000			1:45(105)	J	5963			1.13
164	9 month	F	Pre B ALL	Completed	7800		140000	No growth	N	308	1026	2700	295000			1:30(90)	J	3042			
165	12	F	T cell ALL		11100	11.9	260000	No growth	N	363						1:40(100)	J	9435		still going on	1.03
166	7 month	M	AML		4700	15.1	48000	No growth	Y	356						1:50(110)	S	94	3.7	still going on	1.37
167	10	M	Pre B ALL		3400	10.1	131000	No growth	Y	356						1:55(115)	J	1191		still going on	0.93
168	1	M	Acute leukemia	infection	101000	11.4	370900	N	N	31	220	2200		MRSA	MRSA	1:45(105)	J	4939	4.4	completed	1.04

169	8	M	Neuroblastoma	infection	11500	13.5	408000	N	Y	87	312	5200	6000	No growth	No growth	1:25(85)	J	3335	3.8	still going on	1.23
170	4	M	Pre B ALL		1800	11.9	19000	No growth	Y	5						00:45(45)	J	18	3.6	don't know referred	1.06
171	1	M	Pre B ALL		2800	11.8	10000	N	Y	314						1:45(105)	S	168	3.9	still going on	1.1
172	6	M	Lymphoma		17400		107000	No growth	Y	314						00:50(50)	S	2436		still going on	
173	13	M	Osteosarcoma		8400		260000	No growth	N	314						1:45(105)	J	5292		still going on	
174	0	M	Osteosarcoma	Sepsis fungal	10500	11.1	229000	No growth	Y	140	3498	6600	50000	Aspergillus		2:00(120)	S	6195		don't know referred	1.02
175	3	M	Pre B ALL		1400	12.2	28000	No growth	Y	300						1:30(90)	J	70	4	still going on	1.1
176	1	M	ALL		6800	12.9	15000	No growth	N	300						2:00(120)	J	2788	4.6	still going on	1.18
177	13	M	Ewing's sarcoma		13500	11	251000	No growth	N	259						1:30(90)	J	3645		still going on	1
178	3	M	Pre B ALL		8500	11.2	26000	No growth	Y	259						2:00(120)	J	1275		still going on	1.05
179	2	M	Pre B ALL		4500	10.7	16000	No growth	Y	259						1:15(75)	J	1170	4.2	still going on	0.97
180	1	M	Pre B ALL		21700		35000	N	Y	349						1:45(105)	J	716	4	still going on	
181	2	M	Ewing's sarcoma		10400	10.6	361000	No growth	N	335						00:55(55)	J	4160	3.9	still going on	0.96
182	13	M	Ewing's sarcoma		4000		214000	N	N	335						1:15(75)	J	1680		still going on	
183	8	M	Pre B ALL		51000	13.2	23000	N	Y	335						1:50(110)	J	4508	3.9	still going on	1.21
184	1	F	RMS		16200		369000	N	Y	308						1:10(70)	J	3888		still going on	
185	5	F	Pre B ALL		3300	11.2	64000	No growth	Y	293						1:50(110)	J	664		still going on	1.05
186	2	M	Wilm's	completed	10100	11.7	533000	N	Y	157	2310	7700	330000			1:40(100)	J	3838			1.06
187	4	M	ALL		4300	12.4	15000	No growth	Y	279						1:15(75)	J	19	4.1	still going on	1.13
188	7	M	RMS		4500		306000	N	Y	279						1:40(100)	J	3105		still going on	
189	3	F	Pre B ALL		2900	11	27000	No growth	Y	279						1:40(100)	J	116	3.1	still going on	1
190	2	M	Pre B ALL		2200	12.1	15000	No growth	Y	265						1:15(75)	J	0	4.5	still going on	1.13
191	6month	M	Pre B ALL		5100	12.8	32000	No growth	Y	244						1:15(75)	S	421		still going on	1.09
192	1	F	Lymphoma	Completed	11200	11.5	193000	No growth	Y	229	3528	9800	259000			1:40(100)	J	2576	4		1.06
193	6	M	ALL	Completed	5200	11.9	352000	No growth	N	1322	3060	6800	295000			1:45(105)	S	3276			1.03
194	4	M	Neuroblastoma	Completed	13400		574000	No growth	N	238	3102	6600	293000			1:45(105)	J	7236			
195	5	F	AML		5300		39000	No growth	Y	223						1:30(90)	J	106	4.2	still going on	
196	8	F	ALL	Completed	2700	12.3	257000	No growth	Y	1140	2964	7900	277000			1:15(75)	J	54			1.07
197	9	M	Pre B ALL	Completed	1000	13.4	15000	No growth	Y	1331	3600	7200	231000			1:45(105)	S	20			1.16
198	6	F	ALL		17600	11.1	18000	N	Y	209						1:40(100)	S	299	3.8	still going on	1.01
199	1	M	Pre B ALL		2800	10.6	14000	No growth	Y	202						1:15(75)	J	451		still going on	0.92
200	3	M	Neuroblastoma		3300	11.2	103000	No growth	Y	174						1:15(75)	J	132		don't know referred	1.05
201	15	F	Pre B ALL		1300	10.8	22000	No growth	Y	195						1:50(110)	J	78	4.8	still going on	0.98
202	2	F	AML		24000	11.4	9000	contaminants	Y	19						1:45(105)	J	14880		death	1.04

203	3	M	Pre B ALL		1100	11.4	38000	N	Y	188						1:45(105)	S	110	4.5	still going on	1.04
204	3	F	Neuroblastoma		6700	14.9	158000	N	N	174						1:25(85)	J	3953	4	still going on	1.35
205	7	M	Hodgkin lymphoma		18100	12	440000	No growth	Y	160						1:45(105)	J	14299	3.8	still going on	1.09
206	3	F	ALL	infection	1700	12.7	15000	No growth	Y	12	Not done	200	10000		Staph Coag Neg	1:30(90)	J	17	3.5	death on 22/08/2013	1.16
207	8	M	T cell ALL		6100	14.1	15000	N	Y	146						1:50(110)	J	82	3.7	still going on	1.28
208	2	M	ALL		17800	11.4	20000	No growth	Y	131						1:15(75)	J	356	4.7	still going on	1.04
209	1	M	ALL		7000	13.6	32000	N	Y	95						1:15(75)	J	140		death	1.23
210	9	F	Lymphoma		10200	12	359000	No growth	Y	132						1:15(75)	J	6222	3.1	still going on	1.09
211	4	F	Rhabdoid tumour		8600	11.4	454000	N	N	118						1:15(75)	J	2752		still going on	1.04
212	12	M	Osteosarcoma		10000	11	10000	NFGNB	Y	118						1:15(75)	J	4700	4.5	still going on	1
213	13	F	T cell ALL		1500		247000	N	Y	118						1:15(75)	J	310	3.9	still going on	
214	1	F	Pre B ALL		5300		91000	No growth	Y	2						1:30(90)	J	1166		don't know referred	
215	1	F	neuroblastoma	infection	18200		321000	N	Y	150	Not done	100	9000	No growth	Coagulase neg	1:45(105)	S	4186	4.4	still going on	
216	1	F	AML		147100	10.8	78000	N	Y	90						1:30(90)	J	9143	4.5	still going on	0.93
217	11	M	Osteosarcoma		11600		325000	N	N	76						1:20(80)	J	4950		still going on	
218	7	M	RMS		3100		394000	N	Y	76						1:30(90)	J	1674	4.2	still going on	
219	1	M	Hepatoblastoma		11300	10.6	397000	N	N	177						1:30(90)	J	1808	4.5	still going on	0.92
220	2	M	Pre B ALL		500	12.8	76000	N	Y	139						1:45(105)	J	0		still going on	1.09
221	4	F	Pre B ALL		8800	11.5	12000	No growth	Y	139						0:55(55)	J	1441	4.3	still going on	1.06
222	2	M	Neuroblastoma		3500	11.7	93000	No growth	Y	125						1:30(90)	J	350	4.5	still going on	1.07
223	3	F	Pre B ALL		3900	12.4	21000	Diphtheroids	Y	125						1:25(85)	J	123	4.5	still going on	1.13
224	1	M	Leukemia	infection	3900	21.5	8000	candida tropicalis	Y	23	520	2600	9000	MRSA	MRSA	1:15(75)	J	507	3.4	don't know referred	1.91
225	8	F	Pre B ALL	completed	1600	13.9	39000	No growth	Y	1183	3900	10000	2040000			1:20(80)	S	176			1.21
226	4	M	Pre B ALL	completed	2500	13.1	123000	No growth	Y	1196	611	4700	358000			1:30(90)	S	300			1.15
227	6	F	Neuroblastoma		9400	12.1	224000	N	Y	83						1:00(60)	J	8178	2.5	still going on	1.13
228	11	M	Hodgkin lymphoma		7100		571000	No growth	Y	83						1:10(70)	J	5112		still going on	
229	4	M	Pre B ALL		2000	10.7	212000	No growth	Y	70						1:15(75)	S	800	4.4	still going on	0.97
230	1	F	Wilm's bilateral		16500	11.3	459000	Coag Neg staph	Y	70						1:15(75)	S	13695	2.4	still going on	1.02
231	6month	M	Hepatoblastoma		9700	10.9	424000	N	Y	41						1:20(80)	J	1261	4.3	still going on	0.99
232	4	F	ALL		600	10.7	16000	No growth	Y	181						1:10(70)	J	6	4.3	still going on	0.97
233	2	M	Ependymoma		5100	10.8	167000	N	Y	48						1:30(90)	J	1020		still going on	0.93
234	6	M	Lymphoma		9100	14.8	174000	N	Y	46						1:15(75)	J	6461		still going on	1.34
235	3	F	ALL		9600	11.8	191000	No growth	Y	34						1:10(70)	J	6912		still going on	1.1
236	6	M	Lymphoma		4100	13.9	17000	No growth	Y	34						1:05(65)	J	902	3.7	still going on	1.21

237	3	F	Pre B ALL		6500	11.5	161000	No growth	Y	20						1:00(60)	J	1430	3.6	still going on	1.06
238	3	M	EMS bladder		400	11.7	162000	No growth	Y	20						0:50(50)	J	N	4.1	still going on	1.07
239	7	M	Pre B ALL	completed	1300	12.8	113000	No growth	Y	589	506	2200	263000			1:15(75)	S	39	3		1.09